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MUCOPOLYSACCHARIDES IN HUMAN EPIDERMIS.*

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BOTH neutral and acid mucopolysaccharides have been demonstrated in the epidermis (Stoughton and Wells, 1950; Dupré, 1952; Braun-Falco, 1954; Montagna, 1956; Prunieras, 1957; Steiner, 1958; Braun-Falco and Weber, 1958; Steigleder, 1958, and Flesch, 1959). In 1929, Rothman and Schaaf summarized the findings of earlier authors concerning the nature and importance of mucoid substances isolated from human epidermis. Adam and Korting (1955) extracted material from the normal skin surfaces which gave a positive periodic acid leucofuchsin reaction (PAS). In parakeratotic horny layers, various kinds of PAS-positive substances have been found. Their histochemical behaviour suggests the presence of neutral mucopolysaccharides (Steigleder, 1958a). In addition, material is also present in parakeratotic horny layers which stains with alcian blue (Steigleder, 1958a). Several investigators have demonstrated the presence of components of mucopolysaccharides in both normal and pathological epidermis by biochemical analyses. Parakeratotic horny layers are especially rich in these compounds (Rothman and Schaaf, 1929; Weber and Braun-Falco, 1958; Roe, 1959; Flesch, Roe and Esoda, 1960). It has been shown by histochemical techniques that most of the PAS-positive material present in hyperkeratotic and parakeratotic stratum corneum is bound to proteins (Braun-Falco, 1954, 1958; Steigleder, 1957, 1958a). Histochemical methods, however, do not provide exact enough information to allow classification according to the terminology suggested by Meyer (1945). Due to this lack of a definite classification, different authors use the same term to

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designate chemically different compounds (Gibian, 1959). Therefore, in an attempt to clarify this matter, we shall classify as carbohydrate-protein complexes material which has the following features (Leblond, Glegg and Eidinger, 1957). It is stained by the PAS technique; this staining is due to the presence of 1,2 glycol groups and therefore disappears after acetylation prior to staining; PAS-positivity reappears after acetylation followed by alkalinization; it is stained by the ninhydrin-Schiff-reaction, but not by alcian blue or the Hale technique. Compounds stained blue by the last two methods are termed acid mucopolysaccharides even though neither method, especially the Hale technique, is absolutely specific (Pearse, 1960).

In this paper, both the sources and the importance of the compounds containing carbohydrates bound to protein and acid mucopolysaccharides are discussed.

INVESTIGATION.

Normal skin was obtained from patients undergoing surgery under general anaesthesia. Specimens were incubated in solutions of lithium bromide of several concentrations for various lengths of time. These techniques have been discussed in detail in a previous paper which stressed different aspects of the subject (Steigleder and Weakley, *in press*). Some specimens were stretched according to the method of Van Scott (1952). The epidermis was not separated from the corium after stretching, but allowed to remain in place. Following these treatments the skin was fixed in formalin and imbedded in paraffin. Formalin fixed controls were used.

The histochemical techniques used were as follows. The alcian blue-PAS (Runge, Ebner and Lindenschmidt, 1956) and Mueller's modification of the Hale-technique combined with PAS reaction; performic acid-alcian blue technique for the demonstration of disulphide groups according to Adam and Sloper; demonstration of protein-bound sulphydryl groups according to Barnett and Seligman; Feulgen's nuclear stain following immersion of the sections in hot water (Steigleder and Weakley, *in press*), and thionine, both with and without previous treatment with ribonuclease. The PAS reaction was performed after acetylation, acetylation and alkalinization, and digestion with testicular hyaluronidase. The methods are described in the second edition of Pearse's *Histochemistry* (1960).

RESULTS.

Our findings confirm those mentioned in the introduction concerning the presence of protein bound carbohydrates in epithelial bridges, on the cell surface and in smaller amounts in the epithelial cells themselves. In hyperkeratotic areas, this material occurs between the horny cells. The epithelial bridges are also stained by the ninhydrin-Schiff reaction and by the method of Barnett and Seligman for sulphydryl-groups. They do not stain with the reaction of Adam and Sloper, but are stained by alcian blue and the Hale technique. As stated by Steiner (1958) and Braun-Falco and Weber (1958), this material disappears after previous exposure to testicular hyaluronidase. The prickles are preserved after such treatment. The ninhydrin-Schiff reaction also stains the

PAS-positive material present between the horny cells of the palms and soles and in hyperkeratosis as has been previously described (Steigleder, 1958*b*).

In some specimens, incubation in 2.0 and 3.0 M solutions of lithium bromide or short exposure (10–30 minutes) to a 6.6 M solution caused changes in the material between the cells as stained by alcian blue and the Hale technique. In addition to the stained material occurring in or on the epithelial prickles, as seen in normal skin, more of this material appeared. Even the entire intercellular space was sometimes filled with it (Fig. 1), as in some pathological pro-

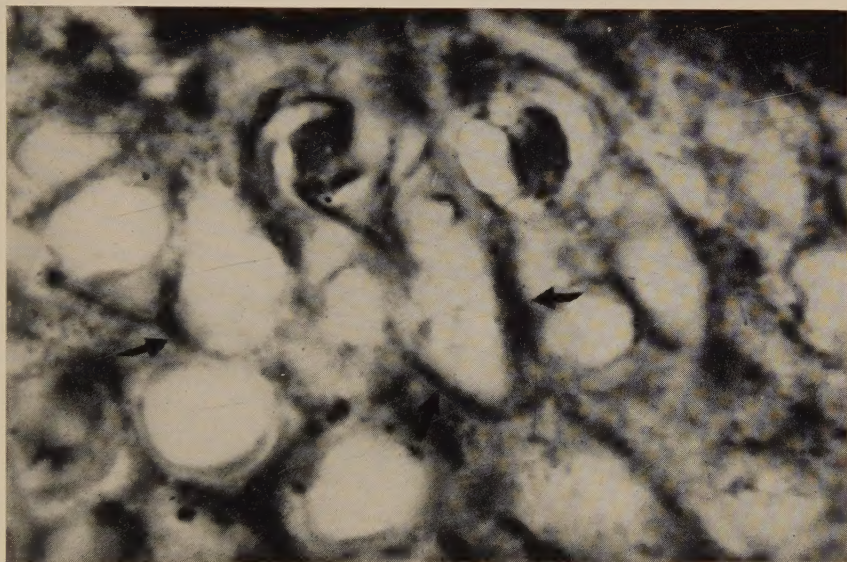


FIG. 1.—Normal skin incubated for ten minutes in a 6.6 M solution of lithium bromide prior to fixation. Note the dark material between the epithelial cells which stains strongly with the Hale technique (arrows). Nuclear shrinkage is also present. The dark material at the top of the section represents both the granules of the stratum granulosum stained by the Hale technique and PAS-positive material. (Hale-PAS, $\times 2500$.)

cesses of the epidermis (Braun-Falco and Weber, 1958*b*). With more prolonged incubation, this material disappeared.

After at least half an hour of incubation in solutions of 6.6 M lithium bromide, whole cells were dissolved. Finally, a homogeneous material replaced these cells and filled the space they formerly occupied or appeared in subepidermal bullae as we have previously described (Steigleder and Weakley, *in press*). This material stained with eosin, the ninhydrin-Schiff reaction, and the reaction of Barnett and Seligman for sulphhydryl groups. It was consistently Feulgen negative. Ribonuclease did not influence the slightly basophilic staining with thionine. The substance also stained with the PAS reaction and had all the histochemical characteristics listed in the introduction necessary for the assumption of the presence of carbohydrates bound to protein.

Stretching of the skin caused the expulsion of PAS-positive material from the ducts of eccrine sweat glands in some specimens (Fig. 2). In addition, PAS-positive material with the histochemical characteristics of protein bound carbohydrates was occasionally found between the stratum corneum and the stratum granulosum. We were unable to demonstrate continuity between any duct of an eccrine sweat gland and this material nor was the material demonstrable in every specimen.

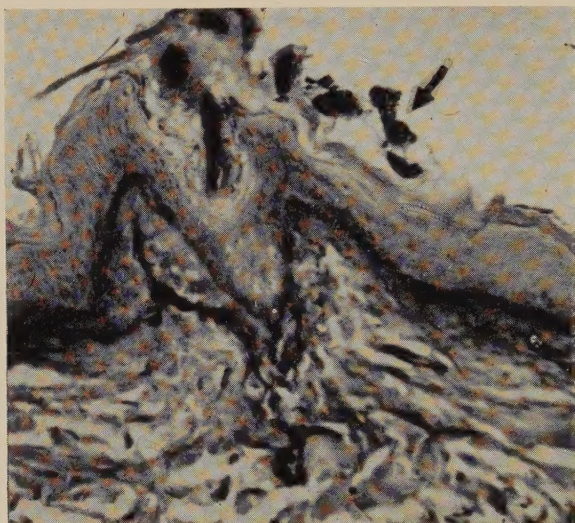


FIG. 2.—Normal skin following stretching. PAS-positive material expelled from the ducts of eccrine sweat glands is apparent. It is distributed on the surface of the stratum corneum. (Hale-PAS, $\times 200$.)

DISCUSSION.

Our histochemical findings confirm those of former investigators in demonstrating that carbohydrates bound to protein and acid mucopolysaccharides are present in normal human epidermis. The former are, in part, neutral mucopolysaccharides bound to proteins. The possibility of other substances being responsible for some of the staining, however, must be taken into consideration (Leblond, Glegg and Eiding, 1957) as will be discussed below. They are present in the epithelial prickles (Dupré, 1952; Braun-Falco, 1954) and also probably cover the entire surface of epidermal cells (Braun-Falco, 1954). These substances have been demonstrated between the cells of the stratum corneum in both hyperkeratosis and in parakeratosis combined with hyperkeratosis (Steigleder, 1958a). Hyperkeratosis is defined as a greater than normal thickness of the stratum corneum, considering, of course, the area in question. PAS-positive substances are found not only between the horny cells of the

stratum corneum of the palms and soles but also on both its upper and lower surfaces. The "wave-troughs" overlying the adhesive ridges (*Haftkaemme*, Petersen, 1935) of the epidermis also stain intensely (Steigleder, 1958b). The result is that large blocks of the stratum corneum are surrounded by carbohydrates bound to protein.

These observations confirm the view that carbohydrates bound to protein may be a cement substance which helps determine the rate of loss of horny cells. Flesch (1959), however, felt that at present there was insufficient evidence that mucopolysaccharides performed such functions in the epidermis. On the other hand, we agree with Braun-Falco (1958) that cementing is probably not their only function. For example, esterase activity is found between horny cells at the sites where PAS-positivity is most marked (Steigleder and Elschner, 1959). Such a connection indicates that the protein bound carbohydrates may play a significant role in maintaining the localization of enzymes in the stratum corneum. Unfortunately, our knowledge of neutral mucopolysaccharides is meagre. However, some of their components, for example glucosamine, probably possess special biochemical importance. The similarity between the chemical structure of this substance and pyridoxamine (vitamin B₆) is striking. Pyridoxamine acts as the co-enzyme of several transaminases, decarboxylases and deaminases (Baldwin, 1959). Neutral mucopolysaccharides appear to have an important function in protecting both the surface of the cornea (Graumann and Rohen, 1958) and the epithelium of the mucous membranes (Odin, 1958). They may act as plasticizers of fibrous protein (Schubert, 1952). Plasticizers are products which are used to modify the mechanical properties of plastics. For this reason it is conceivable that carbohydrates bound to protein are important in determining both the structure and mechanical properties of stratum corneum.

By the action of aqueous solutions of 6.6 and 8.2 M lithium bromide, entire epidermal cells are liquefied. A more or less homogeneous product is then found at the site formerly occupied by these cells and also between the epidermis and the corium. The material is probably a mixture of several different compounds. The large amount which appears, as well as the intensity of its PAS staining, indicates that this PAS-positive, amylase resistant material is not derived from the cell surfaces, epithelial prickles and cementing substance alone. In fact, these structures are relatively resistant to the action of lithium bromide and are often preserved in specimens revealing large subepidermal blisters in which PAS-positive material is found. The observed defects in the epithelial cells clearly indicate that at least a large part of the carbohydrates bound to protein are derived from them and not from the corium.

These findings might be explained by the fact that pentoses derived from nucleoproteins present in both the cytoplasm and the nuclei are liberated and give a positive PAS reaction. Our data suggest that either the free pentoses become bound to proteins or that the solubility of extracted substances, in-

cluding pentoses, is decreased by formalin fixation. The second explanation is unlikely, because it would be expected that any pentoses freed during incubation would diffuse from the tissue into the incubation medium prior to fixation. The first explanation is in accordance with the findings of Szakall (1957) that free pentoses deriving from the nuclei combine rapidly with the free amino groups of amino acids.

These data prove that substances exist in the normal epidermis which will take the PAS stain if they are altered in some way. The most likely alteration would be a process of "unmasking", that is, the making available of portions of a compound's structure that are unreactive under normal circumstances. These substances disappear at the onset of keratinization, probably due either to absorption or to the fact that they are metabolized as sources of energy immediately beneath the level of complete keratinization, i.e. in the stratum granulosum. This supposition is supported by our findings in stretched skin where PAS-positive material occasionally appears beneath the stratum corneum following stretching.

As mentioned, we were unable to find an anatomical connection between this material and the ducts of sweat glands, in which several investigators have reported the presence of a PAS-positive material (Hambrick, 1957; Formisanol and Lobitz, 1957). An histochemically similar substance is also found on the surface of the stratum corneum (Fig. 2) in contrast to the material just discussed which is located beneath it. Because of its histochemical behaviour, the PAS-positive material in the sweat glands must contain protein bound carbohydrate. It may serve a protective function similar to that of mucoid substances secreted by the glands of mucous membranes. It may also be identical to the PAS-positive compound extracted from the skin surface by Adam and Korting (1955).

Concerning pathological skin, our results indicate that the carbohydrate protein complex found in intraepidermal blisters (Asscher, 1955) and even subepidermal bullae is not necessarily derived from either blood serum or from the corium.

The protein bound carbohydrates in psoriasiform parakeratosis originate from several sources and their chemical composition may vary, as former histochemical studies have shown (Steigleder, 1957, 1958a). Of interest in this connection are the protein bound carbohydrates previously designated as PAS-positive material of group V. This material either filled the entire cell homogeneously or occurred as perinuclear granules. Braun-Falco (1959) described the homogeneous material as being similar to droplets of blood serum. The granules are found arranged around the nuclei in parakeratotic cells stripped from the skin surface (see Fig. 4 in Steigleder, 1958a). A PAS-positive compound also appears in acantholytic cells in hyperkeratosis follicularis vegetans (Darier's disease). It is perinuclear and in contact with the nuclear membrane.

Reabsorption is impaired in these cells. Therefore, the PAS-positive material is demonstrable, in contrast to the findings in normal epidermis.

These observations together with the results of our experiments indicate that this type of PAS-positive material in the parakeratotic horny cells is most probably derived from the nuclei and contains pentoses. This explanation is in complete agreement with the biochemical investigations of Grueneberg and Szakall (1957) and of Flesch and Esoda (1959). It is difficult to explain why there is a high pentose content in psoriasiform parakeratosis despite the fact that the nuclei are preserved (Grueneberg and Szakall, 1959). Unpublished histochemical data in Darier's disease indicate that the nuclei in dyskeratotic and parakeratotic horny layers reveal different stages of nuclear breakdown varying from complete preservation to such bizarre remnants as *grains*. Further, attention should be paid to the presence of ribonucleic acid in the epithelial cells, since it also contains pentoses. Ribonucleic acid has been found to be increased in psoriatic epidermis (Steigleder, 1955).

Former studies indicate that acid mucopolysaccharides are present on and between the epithelial prickles (Braun-Falco, 1958; Steiner, 1958), and that they are very resistant to extraction by lithium bromide. These findings prove that they are fixed there by forces other than hydrogen bonds. Protein bound carbohydrate and protein bound sulphydryl groups are found in the epithelial bridges. It would be of great interest to know whether or not the observed reactions were due to the presence of several chemical compounds or if only one substance contained all of the molecules necessary for the observed histochemical reactions. The existence of such a single product would explain controversial findings of Flesch and coworkers on the one hand (1960), and Steigleder (1956) and Siebert (1958) on the other, concerning the relative importance of glucosamine and sulphydryl groups in Gram staining of the epidermis.

The transitory appearance of acid mucopolysaccharides in the intracellular spaces can be produced artificially in pieces of skin, devoid of access to the blood stream. Therefore, they are present in normal skin. Lithium bromide extracts acid mucopolysaccharides from the corium (Steigleder and Weakley, *in press*). Our findings did not suggest that they invaded the intracellular spaces of the epidermis from the corium although this possibility could not be completely excluded. On the contrary our results support the view of Braun-Falco (1958) and Braun-Falco and Weber (1958) that the increased amount of acid mucopolysaccharides in the intracellular spaces of the epithelium is derived from the epidermis. These findings are preliminary and need further confirmation. In thin unfixed frozen sections prepared in a cryostat, the epithelial prickles were easily demonstrable under the phase-contrast microscope and stained with both methylene blue and alcian blue (Steigleder, 1960). Except for the prickles and the cementing substance, the intercellular spaces are devoid of stainable

material other than a compound which stains with Sudan black (Braun-Falco and Weber, 1958).

We are not certain of the role played by the acid mucopolysaccharides of the epithelial bridges. It is possible that they act as a filter for larger molecules as has been suggested for the corium (Blumberg and Ogston, 1958). In low concentration, polysaccharides have a leucotactic effect, while in high concentration they have the opposite (Meier, 1958). In addition, acid mucopolysaccharides are well known inhibitors and activators of several enzymes (Gibian, 1959).

It is hoped that the biological aspects presented here will stimulate interest concerning the function of mucopolysaccharides in the epidermis, which have been studied less than related compounds occurring in connective tissue.

SUMMARY.

New findings on the behaviour of neutral and acid mucopolysaccharides in human epidermis have been presented, special emphasis being given to PAS positive, amylase resistant material.

Possible sources and components of this substance have been suggested.

The literature concerning the etiological role of neutral and acid mucopolysaccharides in human epidermis has been reviewed and interpreted in the light of the new data presented.

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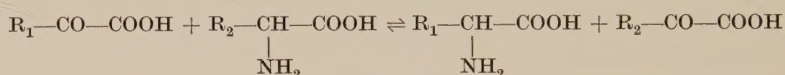
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TRANSAMINASES IN SKIN DISEASE.

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TRANSAMINASES are enzymes catalyzing the transfer of an amino group from an amino acid to an α -keto acid :



The reaction is more specific than is apparent since R_1 or R_2 must possess a carboxylic acid group, i.e. one of the two partners must be a dicarboxylic acid. This virtually means that in transamination a variety of α -keto acids may receive an amino group from aspartic or glutamic acids or a variety of amino acids may give an amino group to either α -keto glutaric or oxalo-acetic acids.

At least two transaminases exist and the reactions they catalyze which are used to measure their activities in clinical chemistry are :

(i) *l*-glutamic acid + oxaloacetic acid $\rightarrow$ *l*-aspartic acid + α -keto glutaric acid.

(ii) *l*-glutamic acid + pyruvic acid $\rightarrow$ *l*-alanine + α -keto glutaric acid.

The enzymes are frequently referred to as SGOT (serum glutamic oxalo-acetic transaminase) and SGPT (serum glutamic pyruvic transaminase). Heart muscle is particularly rich in SGOT and liver cells are rich in both enzymes. When cells die or are damaged, the enzymes leak into the blood stream and can be detected there by the greatly increased SGOT or SGPT activity. These estimations are, therefore, of use in the detection of cardiac infarction and in liver disease and a considerable body of literature exists upon the value of estimation of these enzymes in disorders of the heart and liver. But the enzymes occur in many other tissues and have been demonstrated in skin (Marsilii and Branzi, 1951). Only a few reports have been made on SGOT and SGPT in skin disease. These will be referred to in the discussion. In this paper are recorded the results we have obtained in 194 individuals, some healthy, some with skin disease.

INVESTIGATION.

In Table I are shown the condition, the number of subjects with that condition, the sex distribution and the age range of the group. The majority of the subjects were staff or in-patients of St. John's Hospital for Diseases of the Skin. A few specimens were obtained from the Out-patient Department at St. John's or from Dr. Bettley's clinic at the Middlesex Hospital. The group labelled "photosensitivity" was admitted to St. John's for investigation of light sensitivity and probably forms a heterogeneous collection.

TABLE I.—*Clinical Details of Patients Investigated.*

Condition.	Number of cases.	Males.	Females.	Age Range (years).
Normal	30	14	16	17-60
Psoriasis	25	11	14	17-67
Eczema	25	19	6	17-61
Exfoliative dermatitis	15	11	4	16-74
Atopic dermatitis	25	16	9	13-46
Photosensitivity	9	—	—	—
Seborrhoeic dermatitis	25	18	7	25-69
Lichen planus	11	4	7	30-70
Pemphigoid	3	2	1	51-67
Pemphigus vulgaris	2	1	1	32-48
Discoid L.E.	9	4	5	28-50
Systemic L.E.*	6	2	4	23-57
Mycosis fungoides	3	2	1	49-66
Miscellaneous†	6	5	1	39-83

* All quiescent.

† One case each of dermatomyositis, Hodgkin's disease, epithelioma, dermatitis papulosa nigra, vitiligo and pemphigus foliaceus.

SGOT and SGPT were measured by a simplified version of the method of Wróblewski and Cabaud (1957). Sigma reagents were used throughout.

RESULTS.

Results are shown in Tables II to V. Table II shows results of SGOT in those groups with sufficient numbers for statistical analysis. Column 1 shows the condition in question; column 2 gives the mean SGOT value in units/ml. plus or minus twice the standard deviation of the mean. Column 3 gives the standard deviation of the series and column 4 the probability that the difference observed between the mean SGOT of normal subjects and of sufferers from the particular skin disease could arise by chance. The normal range for our series is taken as the mean plus or minus twice the standard deviation i.e. 5-34 units/ml. It can be seen that only patients with atopic dermatitis and seborrhoeic dermatitis had as groups an abnormally raised SGOT.

TABLE II.—*Results for SGOT.*

Group	Mean (units/ml.)	S.D. (series)	P
Normal	19.5 ± 2.68	7.34	—
Psoriasis	25.3 ± 6.4	16.0	<0.1
Eczema	23.6 ± 3.6	9.19	<0.1
Exfoliative dermatitis	22.7 ± 5.4	10.5	<0.3
Atopic dermatitis	30.4 ± 7.2	18.0	<0.01
Photosensitivity*	37.3 ± 30	45.3	<0.1
Seborrhoeic dermatitis	24.0 ± 3.11	7.79	<0.05
Lichen planus	24.4 ± 4.5	7.45	<0.1
Discoid L.E.	23.0 ± 5.0	7.90	<0.3
Systemic L.E.	19.7 ± 6.1	7.52	>0.9

* Including one grossly abnormal value of 155 units/ml. Excluding this, the group's mean, standard deviation and P are 21.4 ± 6.2 ; 8.72; less than 0.6 respectively.

TABLE III.—*Results for SGPT.*

Group	Mean (units/ml.)	S.D. (series)	P
Normal	10.7 ± 2.0	5.34	—
Psoriasis	17.6 ± 6.1	15.2	<0.05
Eczema	17.3 ± 9.21	—	<0.01
Exfoliative dermatitis	18.6 ± 8.5	—	<0.001
Atopic dermatitis	21.7 ± 7.3	18.3	<0.01
Photosensitivity*	24.2 ± 26.6	39.9	<0.1
Seborrhoeic dermatitis	17.8 ± 3.2	8.11	<0.001
Lichen planus	19.5 ± 5.6	9.31	<0.001
Discoid L.E.	10.5 ± 3.2	5.0	>0.9
Systemic L.E.	9.3 ± 4.5	5.55	<0.6

* Including one grossly abnormal value of 130 units/ml. Excluding this the group's mean, standard deviation and P are 11 ± 4 ; 5.65 and less than 0.9 respectively.

TABLE IV.—*Percentage of Cases with Values Above Normal.*

	SGOT	SGPT	Both.
Psoriasis	28	24	24
Eczema	12	32	12
Exfoliative dermatitis	13	33	6
Atopic	32	36	32
Photosensitivity	22	11	11
Seborrhoeic dermatitis	8	32	8
Lichen planus	9	36	9
Discoid L.E.	0	0	0
Systemic L.E.	0	0	0

TABLE V.—*Results in Miscellaneous Cases.*

Case.	SGOT (units/ml.).	SGPT (units/ml.).
Pemphigoid	25	14
	32	30
	14	10
Pemphigus vulgaris	13	7
	22	13
Mycosis fungoides	14	7
	15	9
	14	12
Hodgkin's disease	18	10
Epithelioma	17	9
Dermatitis papulosa nigra	18	9
Vitiligo	21	8
Pemphigus foliaceus	76	35
{ Dermatomyositis	40	10
{ Same case improved	27	6

Table III is similar to Table II but shows results with SGPT. This enzyme seems more abnormal in skin disease than SGOT since patients with psoriasis, eczema, exfoliative dermatitis, atopic dermatitis, seborrhoeic dermatitis and lichen planus had on the average a raised SGPT. The normal range for SGPT (Mean $\pm$ 2 S.D.) is 0–21 units/ml. although values lower than 5 units/ml. were not seen.

Table IV shows the percentage of patients with various skin diseases having an abnormally high SGOT. Again it can be seen that SGPT is more often abnormal than SGOT and that in those groups which have, as a whole, a raised SGPT about one third of the cases will have individually a raised SGPT. These rises are usually slight, rarely above 50 units/ml. for SGPT or 60 units/ml. in the case of SGOT.

Table V shows results in those conditions in which too few cases were studied to allow statistical analysis. One of three patients with pemphigoid showed a raised SGPT and the only case of pemphigus foliaceus studied showed a rise in both SGOT and SGPT. The single case of dermatomyositis had a raised SGOT which returned to normal as he improved.

DISCUSSION.

Weber (1958 and 1959) studied GOT in serum and cantharidin blister fluid and in scales in thirty patients with skin disease. He found no rise in the enzyme in serum. The activity in blister fluid was several times that in serum, indicating that the enzyme probably occurred in epidermis. Indeed Weber quotes himself as having made the unpublished direct demonstration of GOT in human epidermis. The enzyme is also demonstrable in scales following ultraviolet irradiation and in scales of dermatitis and psoriasis. The activities of the two last are higher than in the first and in psoriasis the scales in active disease show twice the activity of the disease in the healing stage.

Weber and Theisen (1959) have also studied SGPT in twenty cases of dermatitis and nine sufferers from some bullous diseases. Again no abnormalities were seen in serum and in contrast to the findings with SGOT there was little difference between blister fluid and serum in GPT activity, arguing against the presence of the enzyme in epidermis.

De Morages, Perry and Fleisher (1957) have found that SGOT was raised in fourteen cases of active dermatomyositis but was normal in three cases where the disease was inactive, as we also found in our one case. They also found that two of four cases of systemic lupus erythematosus had a raised SGOT.

The present series is by far the largest for skin disease published up to now. We have found that SGPT is more likely to be affected than SGOT, that the mean SGPT is raised in psoriasis, eczema, exfoliative dermatitis, atopic dermatitis, seborrhoeic dermatitis and lichen planus and that the mean SGOT is raised in atopic dermatitis and seborrhoeic dermatitis.

In those groups with a raised mean SGPT, about one third of the cases have an absolutely raised SGPT. Study of these cases and also of those with SGPT does not reveal any factor which could explain why these particular individuals had an abnormal SGPT while others did not. Some were seriously

ill but others were well. Some had extensive skin disease, but others had minimal lesions. A few had other adventitious diseases—gout, hypertension, otitis media—but the majority had not.

However, we have reason to believe that the transaminases are quite labile. One of the authors acted as a control for this series and his SGOT and SGPT were respectively 22 and 28 units per ml., i.e. the latter was raised. The next day, this subject had a raised temperature and an acute respiratory infection. Two months later, when he was healthy, the activities were 14 and 10 units per ml. respectively.

A possible reason for the raised SGPT might be liver dysfunction. However, we have never found abnormal liver function in skin disease unless there was good clinical reason to suspect coincidental hepatic disease.

The dermatologist will not rely upon estimations or serum transaminase to help him in diagnosis. The transaminases when raised, are usually only marginally raised. We think that the only practical importance of our results is to emphasize the fact that where the serum transaminase is estimated in a person with one of a number of skin diseases who is also suspected of having systemic disease, a raised value, if not marked, is of rather less significance than it would be in a normal individual. In dermatomyositis, published work, with which our very limited experience agrees, suggests that estimation of SGOT may be of assistance in determining whether the disease is active or inactive.

SUMMARY.

The SGOT and SGPT were estimated in 30 normal individuals and 164 patients with skin disease.

The mean SGOT was significantly raised in patients with atopic dermatitis and seborrhoeic dermatitis.

The mean SGPT was significantly raised in patients with psoriasis, eczema, exfoliative dermatitis, atopic dermatitis, seborrhoeic dermatitis and lichen planus.

In those cases with a raised mean transaminase, about one third of the sufferers had a raised absolute value of serum transaminase. The rise when present was not great.

The literature on the subjects is discussed and it is concluded that the clinical value of the estimation of serum transaminases in skin diseases is very limited except possibly in assessing activity in dermatomyositis.

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SERUM TRANSAMINASE ESTIMATIONS IN THE DIFFERENTIAL DIAGNOSIS OF COLLAGEN DISEASES.

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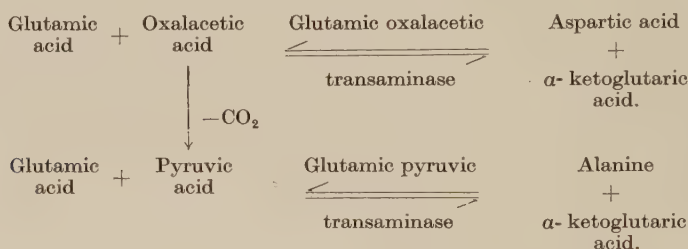
DIFFERENTIATION of the clinical varieties of collagen disorder may be very difficult, especially where dermatomyositis and systemic lupus erythematosus are concerned. Muscle weakness may be only mild in the former and other signs may be common to both conditions. Although treatment is often identical, precise diagnosis is of more than academic importance as the prognosis is very different. In addition, dermatomyositis is associated with internal malignant neoplasia in about twenty-five per cent of cases and may arise long before symptoms appear from the underlying neoplasm.

Differential diagnosis may be easy on clinical grounds alone. Butterfly facial erythema with erythema of the forearms and "V" area of the chest is characteristic of systemic lupus erythematosus, whilst the facial rash of dermatomyositis is more violaceous and in sharp contradistinction to that of systemic lupus erythematosus is concentrated around the eyes. Many patients are seen in whom these differences are by no means so clear cut. Telangiectasia of the nail beds is seen in both conditions and in my experience the changes are identical both clinically and on capillary microscopy. Ingram (1960) has suggested that as a rule the vessels of the nail bed in dermatomyositis are arranged in straight lines, whereas in the majority of patients with systemic lupus erythematosus they form an irregular network. Patients with dermatomyositis often exhibit violaceous streaks on the dorsum of the fingers though these may be confused with chronic discoid lupus erythematosus in a similar site.

The failure of clinical findings to differentiate all cases of dermatomyositis from those of systemic lupus erythematosus has led to the development of many laboratory investigations. Although the L.E. phenomenon has proved of great value (Marten and Blackburn, 1953), the test is negative in a few patients with undoubted systemic lupus erythematosus. L.E. cells may be found in such patients after treatment with cortisone (Haserick, 1951), or ACTH (Marten, 1953). With dermatomyositis the position is even less satisfactory. Muscle biopsy may be negative as there are often islands of normal muscle in even the most florid case (Clein, 1953) and the urinary excretion of creatine and creatinine has been found of little diagnostic value (Christianson *et al.*, 1956). It is

clear that there is need for a sensitive test for the detection of active myositis. With these facts in view it was decided to investigate the value of estimations of serum transaminase in differential diagnosis and in assessing the results of treatment. Several authors have reported abnormal values of serum glutamic oxalacetic transaminase in dermatomyositis (Siekert and Fleischer, 1956 ; de Moragas *et al.*, 1957 ; Moore *et al.*, 1957).

Transaminases are intracellular enzymes and the reactions they catalyze are known to be vital to muscle metabolism (Cohen, 1940) though their exact role is still not fully understood. The enzymes are present in globulins and the processes they catalyze are reversible (Pryse-Davies and Wilkinson, 1958).



The concentration of the two most important transaminases in some important tissues of the human body is shown in Table I. In the present work it is the glutamic oxalacetic transaminase (GOT) that is important as there is a high content of this enzyme in skeletal muscle. When muscle is damaged, 90–98% of the intracellular transaminase is released into the peripheral circulation where it may be detected (Feruglio *et al.*, 1959). It matters little whether the damaging agent be infarction, inflammation or trauma (Siekert and Fleischer 1956 ; Lieberman *et al.*, 1957*a* and *b*), the elevation of serum transaminase that results from any of these processes being proportional to the amount of muscle damaged (Lemley-Stone *et al.*, 1955). An atrophic process such as progressive muscular atrophy does not give rise to elevations of serum transaminase, presumably because the cell wall remains intact (Siekert and Fleischer, 1956).

TABLE I.—*Concentration of Transaminases in Various Sites, from Wróblewski, 1958.*

(as units $\times 10^{-4}$ /g. wet tissue homogenate)

Tissue.	Glutamic oxalacetic transaminase.	Glutamic pyruvic transaminase.
Heart . . .	156	7.1
Liver . . .	142	44
Skeletal muscle . . .	99	4.8
Kidney . . .	91	19
Pancreas . . .	28	2
Serum . . .	0.02	0.016

INVESTIGATION.

Method of estimation.—Ten ml. of venous blood were collected in a sterile bottle containing a few drops of liquid paraffin and allowed to clot at room temperature (never standing longer than one hour). The bottle was then placed in a refrigerator at 0° C. till clot retraction had occurred (about two hours). The specimen was centrifuged and serum placed in a sterile tube with an inert latex stopper. It was then stored at -19° C. till required. Any specimen showing haemolysis was rejected. These precautions were taken because deterioration of enzyme activity occurred rapidly at higher temperatures or after bacterial contamination.

Serum glutamic oxalacetic transaminase was estimated by the colorimetric method of King (1958; 1960) with minor modifications. Special care was taken to control the temperature during the period of enzyme action, which was accurately timed. Results were read in the Unicam spectrophotometer at 5200 Å. Separate standard curves were drawn up for various sizes of cuvette to avoid unnecessary dilution when high levels were recorded and to give greater accuracy in the lower levels by ensuring that the optical densities fell into the most accurate range of the spectrophotometer. Repeatability was of the order of 5% using the standard curves of King (1960).

Clinical material.—Serum from 200 controls was examined to establish a normal range. These were patients attending hospital out-patient clinics after full clinical and laboratory investigations had disclosed no disease likely to influence the transaminase levels, fit medical students or patients attending the Skin Department with warts, moles or other minor skin lesions, with no evidence of general disease.

The vast majority were in the age group from 20 to 40 years and the oldest was 55.

Serum was then examined from a large number of patients suffering from proven or suspected collagen diseases attending the United Sheffield Hospitals and the City General Hospital, Sheffield, between November 1958 and July 1960. Of the patients with dermatomyositis, all except one had serial estimations of SGOT, urinary creatine and creatinine excretion and a muscle biopsy.

RESULTS.

Table II shows the results in the whole series investigated. It was thought important to establish the normal range on a large number of patients, as there is considerable variation in the literature, probably due to minor alterations in technique. The patients suffering from dermatomyositis stand out clearly as the only group with abnormal SGOT levels. Not included in the table are results in one patient who developed dermatomyositis five years ago. Treat-

TABLE II.—*SGOT Estimations in Various Diseases.*

Disease.	No. of patients.	SGOT (King units per 100 ml. serum).		
		Minimum.	Median.	Maximum.
Normals	200	19	49	75
Dermatomyositis	5	124	292	485
Lupus erythematosus (discoid and systemic)	38	24	43.4	64
Scleroderma and acrosclerosis	19	24	49.5	65
Raynaud's phenomenon	14	26	47.4	66
Light eruption	12	18	38.6	54
Dermatitis and eczema	69	19	44.6	59
Rheumatoid arthritis	14	32	50.2	70

ment with systemic steroids was symptomatically successful; the dose of steroid was slowly decreased and, after several normal SGOT determinations, finally stopped. This was followed neither by recurrence of symptoms nor a rise in SGOT levels.

It should be noted that several of the patients with scleroderma and rheumatoid arthritis had marked muscle weakness and wasting but all had normal levels of SGOT, many of them on several occasions.

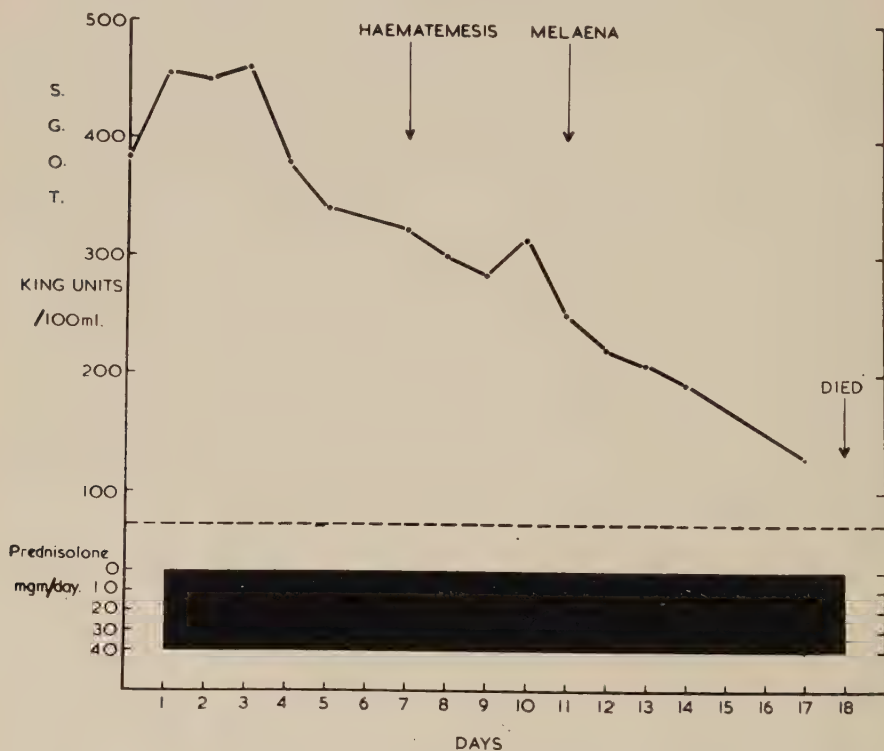


FIG. 1.

Fig. 1 shows the results of serial estimations of SGOT in a man of 61 who had undergone oesophagectomy for adenocarcinoma three years before developing severe, acute dermatomyositis. Treatment with systemic steroids led to loss of muscle tenderness which was associated with increase in muscle power and a fall in SGOT levels. Progress was interrupted by repeated and finally fatal gastrointestinal haemorrhage. Surgical intervention was not attempted as recurrence of the cancer was thought to be the likely cause of haemorrhage. Autopsy, however, disclosed only local recurrence in glands, the fatal haemorrhage occurring from an acute gastric ulcer, possibly related to steroid therapy. It was interesting to note in this patient that urinary creatine and creatinine

excretions were normal at a time when the dermatomyositis was clinically very active and the SGOT level 359 King units per 100 ml.

Fig. 2 shows the results of another series of observations on a patient with dermatomyositis, a woman aged 37 years, who responded well to systemic steroid therapy though her progress was interrupted by a severe pulmonary embolus. Steroid therapy was discontinued at this point in view of the risk of aggravating any tendency to further peripheral venous thromboses and anti-coagulant therapy was instituted. SGOT levels promptly rose to grossly abnormal levels and it was clear that these paralleled the degree of clinical activity, the rise preceding any increase in clinical myositis. Urinary creatine

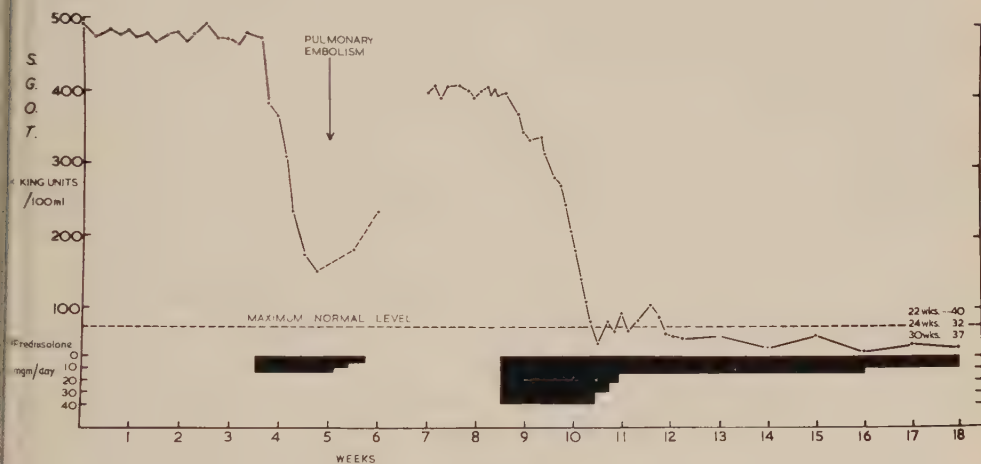


FIG. 2.

and creatinine excretion were studied at intervals throughout the period of observation and bore little relation to other criteria of activity, being normal at times when clinical activity was obvious and SGOT levels high. The latter appeared the most sensitive index of activity. Reduction of steroid dosage was controlled by the SGOT levels rather than clinical signs, as muscle weakness persists long after the myositis is inactive. At no time was reduction associated with clinical deterioration in muscle power.

Four of the patients with dermatomyositis had muscle biopsies, in two the specimens were positive, one showed non-specific changes and the other was negative (this was the most florid case and extensive myositis was demonstrated at autopsy).

In order to test the validity of SGOT levels in the assessment of activity in a patient under treatment with systemic steroids, certain further observations were made. In twelve patients treated with systemic steroids for other dermatological diseases, serial estimations of SGOT were performed before and for

several weeks after starting therapy. In none was any significant alteration in SGOT levels detected.

To demonstrate the effect *in vitro*, increasing concentrations of prednisolone phosphate were added to the substrate used in estimation of SGOT in seven normal and abnormal sera. Only when very high concentrations of prednisolone, equivalent to a dose of 480 mg./day, were added was there any effect on the results; this effect was almost certainly due to alteration in pH (King, 1960). To determine if circulating metabolites of prednisolone had any effect on the test *in vitro*, serum was obtained from a patient taking 80 mg. of prednisolone daily and the SGOT inactivated by incubation at 37° C. for forty-eight hours. At the end of this time, there was no detectable enzymatic activity. Varying concentrations of this serum were then added to the substrate as in the previous experiment. Once again there was no detectable alteration.

DISCUSSION.

The results presented agree with those of Siekert and Fleischer (1956) and Moore *et al.* (1957), who found consistent elevations of SGOT in dermatomyositis and showed that the degree of activity of the myositis could be correlated to the elevation in SGOT. The former authors stated that the effect of the dermatitis on SGOT levels was not known. The present estimations in a large number of patients with dermatitis and eczema establish that elevations of SGOT do not occur from dermatitis alone; this is in keeping with the low levels of GOT found in skin. Moore *et al.* (1957) and de Moragas *et al.* (1957) also showed that the raised SGOT levels fell after treatment with systemic steroids. The latter authors believed the test to be of little value in differential diagnosis, as two of their patients with systemic lupus erythematosus had increased SGOT levels; both were suffering from clinical myositis. It seems possible that the true diagnosis in these two patients was dermatomyositis, as there are reports of patients originally thought to have systemic lupus erythematosus who later clearly suffered from dermatomyositis (Marten and Blackburn, 1956). It is of interest that O'Leary *et al.* (1955), who studied histological changes in the muscles of patients suffering from dermatomyositis, found the lesions to be quite different from those in patients with systemic lupus erythematosus or scleroderma where the pathological process is atrophic rather than inflammatory.

The differential diagnosis between dermatomyositis and scleroderma may be as difficult as that between dermatomyositis and systemic lupus erythematosus. Here again, SGOT levels are a great help, abnormal levels never being found in scleroderma in the present series nor in any other (de Moragas *et al.*, 1957; Moore *et al.*, 1957). This is once more a reflection of the difference between an atrophic and an inflammatory process, some break in the continuity of the cell

will being necessary before transaminase is released into the circulation in large amounts.

Of even greater interest and practical importance is the use of serial estimations of SGOT in following the progress of dermatomyositis, whether improvement be spontaneous or due to therapy. One of the great difficulties in assessing progress is the differentiation of continuing mild activity from the effects of quiescent myositis. It is to be expected that a test measuring an enzyme that is only released when muscle is damaged would be of great value. In the present series this is most clearly shown in the patients whose progress is illustrated in Fig. 2, SGOT levels falling to normal when muscle weakness was still marked, yet slow reduction of steroid therapy was not followed by increasing muscle weakness as might be expected if the myositis was still active. Even more striking in this context is another woman of 37 who was first seen seven years ago with a six year history of a violaceous eruption on the dorsum of the fingers and hands, unaccompanied by muscle weakness. A diagnosis of chronic discoid lupus erythematosus was made. There was no response to antimalarial drugs and a skin biopsy showed only a non-specific dermatitis. Gradually a violaceous erythema spread over her face and forearms and, despite the absence of muscle weakness or tenderness, a normal urinary creatine and creatinine excretion and a negative muscle biopsy, a diagnosis of dermatomyositis was made and this was later accepted by the Dermatological Section of the Royal Society of Medicine. Estimations of SGOT have been made on her on seven occasions recently, five were grossly abnormal and the other two above the upper limit of normal. There is still no clinical evidence of myositis other than slight wasting, nor any increase in urinary creatine and creatinine excretion. This seems to demonstrate the extreme sensitivity of the test in detecting myositis and can be compared with the use of SGOT levels in the diagnosis of subclinical myocardial infarction (Burstein and Harjanne, 1959).

There can be little objection to the use of serial estimations of SGOT in assessing the progress of untreated dermatomyositis, but there are two possible objections to this in patients under treatment with systemic steroids. First, the test is a delicate estimation of enzyme activity *in vitro* which is easily deranged by deviations from the strict conditions of time, temperature and pH under which it is performed (King, 1960). It is, therefore, reasonable to argue that the test may be influenced by circulating steroid hormones or their metabolites. It was for this reason that experiments were conducted in which varying concentrations of prednisolone phosphate were added to the substrate used in the test. No effect on the results was demonstrated in seven normal and abnormal sera till a very high concentration was reached equivalent to a dose of 480 mg. daily of prednisolone in an average person. The effects that occurred even at this stage were almost certainly due to a drop in the pH of the substrate which could not be corrected. A second experiment, using serum

obtained from a patient on very high steroid dosage, also failed to demonstrate any effect on the test, in the same group of seven sera from circulating metabolites of steroid hormones. It is, therefore, reasonable to reject the first objection.

The second objection is that systemic steroid therapy may interfere in some way with either production or release of transaminase without actually influencing the underlying process, especially as some authors have reported that steroid therapy does not influence dermatomyositis (Wedgwood *et al.*, 1953). It seems probable that these authors and others were either using doses of steroids which would now be considered inadequate, or treating the more chronic form of the disease where the myositis may be quiescent (McElligott, 1956). There is experimental evidence to show that systemic steroid therapy profoundly influences intracellular transaminase concentrations. Rosen *et al.* (1958 ; 1959) and Gavosto *et al.* (1957) demonstrated increases in intracellular glutamic pyruvic transaminase in the liver of experimental animals treated with systemic steroids. The evidence with regard to GOT is conflicting, Rosen *et al.* (1958) finding no alterations in intracellular levels of this enzyme in similar circumstances, whilst Gavosto *et al.* (1957) found increases in GOT as well as GPT. None of these workers reports results in serum so that conclusions that can be drawn with relation to the present work are somewhat indefinite. It appears possible that acceptance of falling levels of SGOT as evidence of the therapeutic effect of systemic steroid therapy in liver disease is fallacious (O'Brien *et al.*, 1958). Drugs other than steroids have been shown to influence SGOT levels in man, aspirin (Manso *et al.*, 1957), chlorpromazine (Wróblewski and Manso, 1958) and codeine (Foulk and Fleischer, 1957) have all been shown to cause elevations of SGOT, though it is possible that this only occurs in the presence of subclinical liver disease.

The evidence with reference to this second objection that has been obtained in the present series is both incomplete and indirect. No effect on SGOT has been shown in a series of dermatological patients with normal SGOT levels treated with systemic steroids and one patient has been observed who sustained a myocardial infarction whilst on systemic steroids. Serial estimations of SGOT were made and the rise was commensurate with clinical and electrocardiographic prognostic criteria (LaDue and Wróblewski, 1955). Only a series of animal experiments can elucidate this point completely and it is hoped to undertake these in the future.

SUMMARY.

The difficulty of differential diagnosis between dermatomyositis and systemic lupus erythematosus is discussed and the value of estimations of serum glutamic oxalacetic transaminase (SGOT) is demonstrated. It is suggested that this

test detects subclinical degrees of myositis and is therefore valuable in the assessment of activity of the myositis.

There is shown to be no increase in SGOT levels in scleroderma and rheumatoid arthritis, despite great muscle wasting.

Certain theoretical objections to the use of this test in assessing the response of dermatomyositis to systemic steroid therapy are discussed and shown to be invalid, though it is as yet unproven whether such therapy has any effect on the production or release of transaminase from damaged cells. Such an effect seems unlikely from the result obtained so far.

I should like to thank Dr. I. B. Sneddon for constant advice and encouragement throughout this work, and for referring patients to me. Dr. R. E. Church, and the Physicians and Surgeons of the United Sheffield Hospital and City General Hospital, Sheffield, also kindly allowed me to examine patients under their care. I am especially grateful to Dr. A. W. D. Leishman, who allowed me access to his out-patient clinic to obtain normal control sera, and to Drs. R. W. Meikle and H. L. Mathews who supplied me with many abnormal sera for experimental purposes. Dr. Arthur Jordan and Dr. J. R. Daley have helped with much biochemical advice, and Dr. D. S. Munro has been helpful with advice with regard to the experimental work. I am indebted to Mr. Keith Browne, F.I.M.L.T., for much technical advice and to Mr. A. S. Foster, Medical Artist to the United Sheffield Hospitals, for the illustrations.

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ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. HUGH GORDON.

20 October 1960.

Thomson's Syndrome (Poikiloderma Congenita).—Dr. ROBERT WARIN.

A boy aged 4 years.

History.—When 6–7 months old, the eruption appeared over the face, and spread to the backs of the hands, outer aspect of the forearms and dorsum of the feet. It has persisted, but has not increased. Initially exposure to sunlight caused slight redness and scaling but this has not occurred recently. Crops of blisters develop on the feet in the winter. The arms and legs were noticed to be spastic shortly after birth.



FIG. 1.

Family History.—Mother's pregnancies : (i) 1952 miscarriage. (ii) 1954 premature and died at 9 months. Said by the mother to be spastic and to have looked like the patient. (iii) (patient) threatened miscarriage at six weeks. Normal birth.

On examination.—The eruption over the central forehead, cheeks, ear tips, point of chin, outer aspect of forearms, backs of hands and dorsum of feet consists of red, slightly scarred areas with telangiectasia (Fig. 1). Blisters on the borders of the feet have been observed and were $\frac{1}{2}$ –1 cm. diameter, clear with a slightly red margin. There is rigidity of legs and to a less extent arms. Intelligence quotient 80.

Investigations.—Urine negative for phenyl-pyruvic acid, amino-acid chromatography normal. Urine and faeces show no excess of porphyrins.

Comment.—Various congenital defects have been described in association with Thomson's syndrome including bony abnormalities, microcephaly, mental deficiency, cataracts, and abnormalities of hair, teeth and nails, but I have not been able to find any mention of such a spasticity as is present in this boy. The relationship to sunlight is interesting and a number of authors including Whittle (1953), Rook, Whimster (1949) and Brain (1953) mention that these patients were irritated by sunlight in the first few years and not later. Blisters have also been described by Kindler (1954) and Brain (1953). These have often occurred on the feet.

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Pseudo-acanthosis Nigricans.—Dr. R. J. CAIRNS.

A housewife aged 39.

History.—1948 : soon after her third pregnancy she had a sudden gain in weight from 11 to 13 stones. At the same time the sides and back of the neck became dark and thickened.

1950 : after a fourth pregnancy a further gain in weight to 16 st. 12 lbs. was accompanied by more darkening of the neck and the development of pedunculated "warts" in the same region. The axillae and groins became dark and thickened at this time.

1960 : on a strict diet since April she has lost 2 stones with distinct involution of the affected areas, especially those on the thighs.

Menses have been regular and recommenced within one or two months of each delivery.

On examination.—Rather obese, pale woman (weight now 14 stones). General examination normal. Buccal mucosa normal.

Neck : back and sides show some darkening and corrugation. A few skin tags are present, with depigmented areas at the sites of cauterisations. Axillae : both show almost plaque-like hyperkeratosis with some pigmentation. Groins : still some thickening and pigmentation. Antecubital, submammary, umbilical areas normal.

Investigations.—Blood count and E.S.R. normal. Skiagram of skull normal. 17-ketosteroids 7.4 mg./24 hours. Hydroxycorticosteroids 9.6 mg./24 hours.

Histology (left axilla) : changes characteristic of acanthosis nigricans (Dr. H. Haber).

Comment.—There appear to be three distinct varieties of acanthosis nigricans : the juvenile type which is a genodermatosis ; the well known type associated with malignancy and that, sometimes called pseudoacanthosis nigricans, in which the lesions are just as real and histologically typical as in the other varieties, but where the process may be reversible and is often associated with obesity or frank endocrine disorder. The endocrine disorders include Cushing's syndrome, acromegaly, Fröhlich's syndrome and Addison's disease. This patient has no endocrine disease and improvement has coincided with weight reduction.

Dr. B. TATE : Why should we call this condition pseudo-acanthosis nigricans ? Surely acanthosis nigricans is a clinical and pathological concept of changes in the skin. We know that certain cases are associated with malignant disease and others are not, but the histology of the skin is that of acanthosis nigricans in both. We might as well apply the same principle to dermatomyositis, calling those cases not associated with malignancy *pseudo-dermatomyositis*. I think it is the wrong outlook.

Dr. LOUIS FORMAN : Dr. Helen Curth has very fully investigated and established the criteria of benign, pseudo, and malignant acanthosis nigricans. The benign type begins in infancy or in childhood, becomes accentuated at puberty, and either remains stationary or improves with age. She found that there is no malignant association but a definite genetic, sometimes dominant inheritance. Pseudo-acanthosis nigricans, limited to the flexures of the axillae or between and beneath the breasts she associated with obesity, and this improved when the obesity was reduced. There is no genetic background. Acanthosis nigricans of adults may precede the appearance of malignancy by several years. In her review, she notes one patient with acanthosis nigricans in which this latent period was 18 years before the onset of cancer. Even in adolescents, Gougerot has emphasized the importance of observation of the patient for the development of cancer. In the malignant acanthosis nigricans the skin may show isolated warty hypertrophy rather than skin tags.

REFERENCES.

- CURTH, H. O. (1959) *Arch. Derm. Chicago*, **79**, 55.
 ——— (1955) *Ibid.*, **71**, 95.

Rheumatoid Arthritis with Papulonecrotic Arteriolar Lesions on Fingers and Elbows.—Dr. R. J. CAIRNS.

A man aged 53, electrician.

History.—1955 : pain and swelling appeared in various joints, including the fingers. Given butazolidine for over a year, but anaemia and melaena developed and the drug was discontinued. 1957 : vasospastic attacks in the fingers, tests for cryoglobulins and cold agglutinins were negative, vasodilators prescribed. In June 1959 he was given prednisone 5 mg. daily ; after two months, triamcinolone 6 mg. daily. October 1959, papular lesions appeared on the pulp surfaces of the fingers, with violaceous papulonecrotic lesions on the elbows. The tenderness of the finger papules was often intense and quite disabling. Subcutaneous nodules suddenly appeared below the elbow. February 1960, neuritic pain in the left arm was considered to be a "rheumatoid neuropathy". Recently lesions on dorsa of toes have appeared and new ones continue to appear on the fingers. They begin as tender, pinhead sized, dermal papules which become higher and then after some weeks depressed in the centre. Some last only two to three weeks, others up to six weeks. The elbow lesions, however, resolve slowly.

On examination.—Fingers : milium papules in various stages of evolution. Elbows : over extensor surfaces, grouped violaceous papulonecrotic lesions. Subcutaneous nodules over the upper third of ulna.

Investigations.—Full blood count showed moderate anaemia. E.S.R. usually 50 to 100 mm. Protein electrophoresis : increase in γ globulin. L.E. cells present on one occasion (December, 1959). Latex test positive.

Histology (finger nodules 24/48 hrs. old) basophilic colloid degeneration ; (elbow lesion 2 months old) advanced stages of the same process with ulceration. (Dr. H. Haber.)

Comment.—In rheumatoid arthritis there appears to be a variety of vascular lesions. Involvement of larger vessels, with intestinal infarction, gangrene of the extremities or peripheral neuritis, is not likely to present to the dermatologist. Arteriolar involvement, with finger lesions such as these, were described by Bywaters. The connection between arterial involvement and steroid therapy is debated by the rheumatologists. There seems nothing in this case to suggest that steroids might have induced or accelerated the vascular changes. Triamcinolone 20 mg. or more daily, will prevent new lesions appearing, and there is no suggestion of rebound when the dose is decreased. This type of rheumatoid arthritis may show clinical, biochemical and immunological overlap with systemic L.E. and the presence of the L.E. phenomenon on one occasion in no way alters the diagnosis.

Dr. D. S. WILKINSON : I think this a comparatively rare manifestation of the vascular changes that occur in rheumatoid arthritis. I have seen exactly the same lesions on a woman's elbows,

although this patient was on steroids. It has been stated that they occur more frequently in patients on steroid therapy and the lesions certainly become worse when these are left off. Dr. Dudley Hart has written up a series of cases in which he emphasizes sensory nerve changes that he attributes to a vasculitis affecting the small nerves. The more common lesions on the legs are probably infarcts and are similar to those in the group of patients which Dr. Bettley showed at this Society. The patients often have severe rheumatoid arthritis, and the prognosis seems rather worse than usual. Whether this links with the rather frequent finding of a positive L.E. phenomenon I do not know. Whether we are dealing with some intermediate condition or not, I think we should still call the disease rheumatoid arthritis.

The PRESIDENT: Am I right in supposing that steroids make the pain worse?

Dr. WILKINSON: I think that is accepted.

Dr. LOUIS FORMAN: The late Dr. Barber demonstrated under the title of the "arthritis of Poncet" a case of synovial swelling of the elbows and proximal interphalangeal joints of the rheumatoid type and distribution, associated with papulo-necrotic lesions of the hands. Dr. Barber regarded both conditions as tuberculous. However, Prof. Bywaters has described cases of rheumatoid arthritis with tiny tender haemorrhagic and necrotic nodes on the fingers, presumably due to vascular occlusions.

REFERENCE.

PONCET, A. (1897) *Gaz. Hôp.*, **70**, 1270.

The following cases have been published in *Proc. R. Soc. Med.*, **54**, 217.

Melkersson-Rosenthal Syndrome.—Dr. R. J. CAIRNS.

Lichen Myxoedematosus.—Dr. OLIVER SCOTT.

Reticulosis? Xanthoma Disseminatum.—Dr. C. H. WHITTLE and Dr. BRIAN WOODS.

The following cases were also shown.

(i) **Porphyria Cutanea Tarda.** (ii) **Pityriasis Lichenoides Acuta.**—Dr. R. J. CAIRNS.

(i) **Familial Erythrocyanosis Frigida Crurum Puellarum,** (ii) **Dermal Atrophy.**—Dr. P. HALL-SMITH.

Mast Cell Naevus.—Dr. BRIAN F. RUSSELL.

Acrodermatitis Chronica Atrophicans.—Dr. N. A. THORNE.

Pemphigus Foliaceus.—Dr. N. S. SAHA for Dr. E. COLIN-JONES.

Folliculitis Ulerythematosia Reticulata.—Dr. D. SHARVILL.

17 November 1960.

Multiple Glomus Tumours.—Dr. R. J. CAIRNS.

A schoolgirl, aged 15.

History.—Two years ago a painless purple nodule appeared on the right thigh. Since then further nodules have appeared and continued to do so during a period of four months' observation.

On examination.—On the front of the right thigh, surrounding a rather keloidal scar, are about a dozen, small, almost impalpable, violaceous papulonodules. They are usually painless on pressure, but from time to time she is conscious that even the pressure of a suspender will cause pain.

Histology.—In the mid-cutis is a lobulated tumour consisting of large vascular spaces lined by a single endothelium. The walls are studded with masses of cells, arranged in parallel with blurred outlines of their cytoplasm, containing dark stained round nuclei. Tangential sections of some walls of the vessels give the impression of solid tumour formation. The cells have undergone mucinous degeneration. This is a glomus tumour of the telangiectatic variety (Dr. H. Haber).

Dr. I. B. SNEDDON: Dr. R. Church and I described a case similar to the present one some years ago as familial hamartoma. We did not recognize that the lesions were glomus tumours. We dealt with them successfully by diathermy.

REFERENCE.

CHURCH, R. and SNEDDON, I. B. (1954) *Brit. J. Derm.*, **66**, 244.

Rosacea? Rosaceous Tuberculide (Lewandowsky).—Dr. I. MARTIN-SCOTT.

A woman aged 54.

History.—Since March 1960 she has had a permanent flushing of the face, whereas previously her skin was pale and sallow. Menstrual irregularity : had taken Mepilin for some eight years to control this, and also tab. Ergotoxin Co. for her severe headaches. She had also been given mild sedatives—Amytal gr. $\frac{1}{2}$ t.i.d.

No serious illnesses. Her brother had pulmonary tuberculosis in India during the War, when she was in England, and apparently it was mild. There is no other family history of tuberculosis. She has had no digestive or eye symptoms.

On examination.—On the lateral aspects of the cheeks and down the sides of the neck anteriorly there is a fine bluish pin-point papular eruption with some fine dry scaling. The follicles are not patulous and there is no erythema. The scalp is normal. On diascopic pressure the papules are light brown.

The appearance does not suggest either rosacea or a contact dermatitis but a lupoid eruption even in the absence of scarring.

Investigations.—Skiagram of chest normal, Mantoux 1/1000 and 1/100, human and bovine, negative : serum proteins, electrophoretic analysis, normal, A/G ratio 2.

Histological report : Scattered through the corium are collections of endothelial cells and in some are giant cells mainly of Langhan's type. There is a surrounding lymphocytic infiltration and a heavier infiltration of the adjacent corium. Acid-fast bacilli have not been demonstrated. Appearances consistent with diagnosis of rosaceous tuberculide. (Charles Pike.)

Clinically the distribution and morphology of the eruption fits well with that of the rosaceous tuberculide of Lewandowsky, but according to those who have written on the subject, patients should not be so diagnosed unless there is a history of active tuberculosis, or a highly sensitive tuberculin response. This patient did not react to P.P.D., bovine and human, even at a dilution of 1/100. This negative Mantoux reaction is usually found in lupus miliaris disseminatus faciei, a condition in which the lesions usually appear in crops as in a true tuberculide and are disseminated over the face, often involving the eyelids and naso-labial folds, and frequently break down to leave scars.

In spite of the age of onset and the history of flushing of the cheeks, I do not feel that rosacea is the correct diagnosis. In rosacea the central third of the face is usually affected and it is associated with vasodilatation and an excessive sebum secretion—these are absent here.

Most dermatologists who have studied this disease described by Lewandowsky and have done contra-lateral biopsies stress the insignificance of the histological findings, which should not form a basis for a diagnosis. In this present case the histological picture is a distinctive one, and I consider should be taken into account when forming a diagnosis.

The biopsy, which was taken in August 1960 from the skin over the left lower jaw, shows no evidence of rosacea, and the tuberculoid foci are not perifollicular. These discrete foci show a nest of endothelial cells, without any central caseation, surrounded by a lymphocytic halo and some Langhan's giant cells. This picture surely suggests sarcoid, which is in fact the histological picture found in Lewandowsky's rosaceous tuberculide.

I should like to stress, that after considerable study of the literature on this subject, there appears to be a distinct group of cases that conforms with the clinical and histological description by Lewandowsky, but are not true tuberculides. These cases differ from rosacea in that they involve the lateral aspects of the face and neck, the

morphology is one of uniform tiny papules which do not form pustules or scars. They have the histology of sarcoid, no evidence of tuberculin sensitivity or active tuberculosis.

Dr. C. D. CALNAN: Many patients have been treated with INAH and streptomycin but are not reported because these drugs have had no beneficial effect. I think it is unnecessary to maintain his term of Lewandowsky's. Most people now accept Michelson's view that these cases are micro-papular rosacea, even though they show tuberculoid histology.

Neurofibroma.—Dr. S. C. GOLD.

A girl aged 12, Maltese.

History.—At the age of two a raised area the size of half a crown was excised from her back, at the same time a tumour inside the upper lip was removed.

There has been a recurrence of the lesion on her back which over the last year has doubled its size. The girl is said to be unwell, complains of pain in her back and general weakness.

Family history.—Nothing relevant has been discovered in other members of the family but only her mother has been examined.

On examination.—Numerous *café-au-lait* patches and darker pigmented moles are scattered over the skin surface. The fleshy tumour on the back has a warty surface but is compressible in part. There is a discrete firm nodule to be felt (the size of a plum) in the main mass. The base shows some vascularity. The scar runs into the tumour. There is a small gland in the right groin.

Comment.—I brought this girl to the meeting without histological confirmation that the tumour is a solitary neurofibroma. It is not unusual for such lesions to increase rapidly in size around the age of puberty but the fact that this one has regrown after excision so rapidly and extensively made me wonder if it has undergone a sarcomatous change.

Postscript.—The tumour proved to be a neurofibroma and there was no evidence of malignancy.

The following cases have been published in *Proc. R. Soc. Med.*, 54, 220.

Lipoid Proteinosis (Urbach-Wiethe).—Dr. M. A. COWAN for Dr. H. R. VICKERS.
Psoriasiform Dermatoses Associated with Bizarre Metabolic Abnormalities.—Professor C. E. DENT and Dr. M. GARRETT.

Hyperkeratotic Follicular Plugging with Alopecia Totalis.—Dr. R. D. SWEET.

The following cases were also shown.

Borderline (Dimorphous) Leprosy.—Dr. P. J. HARE and Dr. W. H. JOPLING.

Reticulosis.—Dr. M. GARRETT.

Poikiloderma with Reticulosis.—Dr. A. W. MCKENZIE for Dr. H. J. WALLACE.

Case for Diagnosis. ? Granuloma Annulare.—Dr. R. H. CHAMPION for Dr. H. J. WALLACE.

Kyrle's Disease.—Dr. R. J. CAIRNS.

Pseudoxanthoma Elasticum.—Dr. JOHN MORGAN.

Dermatofibrosarcoma.—Dr. I. MARTIN-SCOTT.

Keratosis Punctata.—Dr. K. M. WITHAM.

(i) Scleroderma, (ii) Poikiloderma.—Dr. F. RAY BETTLEY.

15 December 1960.

Keratosis Pilaris with Cicatricial Alopecia and Bilateral Congenital Cataract.—Dr. PETER BORRIE.

A girl aged 18, clerk.

History.—Bilateral cataract and follicular ichthyosis, have been present since

birth. Alopecia began at the age of 10 and progressed for five years. Since then it has been stationary. No relevant past or family histories.

On examination.—Bilateral anterior polar cataracts. Diffuse cicatricial alopecia with some follicular hyperkeratosis. Patchy follicular hyperkeratosis of neck, back, extensor aspect of upper arms and legs. There is loss of hair within the hyperkeratotic areas but no atrophy. The teeth are normal.

Treatment.—Vitamin A 200,000 units t.i.d. for a year. U.V.L. and high-frequency current weekly for two months without any improvement.

Comment.—Keratosi pilaris was first described by Brocq. Although cicatricial alopecia is a recognized accompaniment, I have been unable to find any report of an associated congenital cataract. This is the second patient in whom I have seen this particular ocular complication, which suggests that it is more than a coincidental finding.

Case for Diagnosis ? Subcorneal Pustular Dermatosi s ? Psoriasis.—Dr. M. SMITH.

A man aged 58, clerk.

History.—Jan. 1957, rash in axilla for one week. Nov. 1957 itchy rash on lower trunk, buttocks and thighs, with red-purple papular scaly dry lesions which gradually enlarged to become annular and polycyclic with healed pigmented centres. No new lesions appeared after Jan. 1958 and by March 1958 only pigmentation remained. No further trouble until May 1960 when a similar eruption appeared involving axillae, lower trunk, hips, buttocks, arms and legs.

Family history.—One sister aged 60 has had skin trouble for ten years.

On examination.—Many annular and polycyclic papular scaly purplish lesions up to several centimetres in diameter, some with small erosions on the surface, others with healed pigmented centres, involving the axillae, lower trunk, hips, buttocks, arms and legs. No mucosal lesions.

Investigations.—No mycelium in skin scrapings. Patch Tests with iodine and potassium iodide were negative. Histological examination showed a subcorneal lesion.

Dr. D. S. WILKINSON : I find it hard to accept this case as an example of the rather narrowly defined disease originally described. Inevitably the description of any entity widens with the passage of time, but I think that in this disease it becomes too wide when no pustules are visible. I do not think the histological finding of polymorphonuclear cells is sufficient, histologically speaking, to fulfill the original criteria. The patient has patches of psoriasis on the elbows and scalp.

Dr. M. SMITH : Dr. Borrie (Scott, 1960) had a patient who presented a similar clinical picture to this one and who, after several years, developed typical subcorneal pustular dermatosis.

REFERENCE.

SCOTT, A. (1960) *Proc. R. Soc. Med.*, **53**, 383.

The following cases have been published in *Proc. R. Soc. Med.*, **54**.

Diffuse Systemic Sclerosis.—Dr. P. F. BORRIE.

Pemphigoid with Malignant Melanoma.—Dr. J. M. MARKS for Dr. S. GOLD.

The following cases were also shown.

Urticaria Pigmentosa.—Dr. R. M. B. MACKENNA.

Acne Conglobata.—Dr. P. F. BORRIE.

(i) **Reticulosis**, (ii) **Dermatitis Herpetiformis.**—Dr. A. SCOTT.

Scleroedema (Buschke).—Dr. HAROLD WILSON.

Atrophic Lichen Planus and Pseudopelade.—Dr. C. M. RIDLEY for Dr. BRIAN RUSSELL.

NORTH OF ENGLAND DERMATOLOGICAL SOCIETY.

Sheffield, 12 April 1960.

Tylosis Palmaris et Plantaris.—Dr. I. B. SNEDDON.

A woman aged 33.

History.—Lesions on the feet since age of three years and on the hands only in the last five years.

Family history.—Father had a similar condition. One leg was amputated in 1945 for a squamous epithelioma of heel. Two brothers unaffected.

Examination.—Localized hyperkeratotic plaques on heels and soles. More diffuse hyperkeratosis of the hands, particularly on friction areas.

Investigations.—Histological examination shows hyperkeratosis and acanthosis of the epidermis, and patchy lymphocytic infiltration in the dermis.

Plastic surgery has been suggested in view of the history of neoplasia in the similar condition of her father.

Anetoderma (Jadassohn).—Dr. R. E. CHURCH.

A girl aged 12.

History.—One year ago, onset of purplish spots on the neck which have faded leaving scars. Since then further crops of lesions have appeared on the arms and legs.

Past history.—Migraine for nine months.

Family history.—Nothing relevant.

Examination.—Scattered atrophic macules on the neck with "raisin pouting" of skin. Scattered atrophic macules on the arms and legs. On the calves a few purple macules without atrophy. No *café au lait* stains or nodules.

Histology.—A purple non-atrophic nodule shows non-specific perivascular infiltrate in upper dermis. The centre of the biopsy specimen shows some diminution in the number of elastic fibres in the upper dermis.

Blood count and E.S.R. normal.

Waldenström's Hyperglobulinaemia.—Dr. S. M. TIGHE for Dr. I. B. SNEDDON.

A woman aged 18.

History.—For 2 years she has developed recurrent crops of purpura every 7–10 days, confined mainly to the legs and occurring particularly after prolonged standing or exercise, although not abolished completely by rest. She also has menorrhagia. For 7 years she has had recurrent swellings of the parotid glands.

Past history.—Eight years ago, she had a very severe illness and was in the Children's Hospital for 7 months with gross oedema and albuminuria, a chest infection and, later, a pelvic abscess which drained spontaneously *per rectum*.

Examination.—Purpura on legs and thighs only, lesions 2–3 inches in diameter.

Investigations.—Platelets 250,000/cu. mm. E.S.R. 50 mm. in 1 hr. (persistently elevated at this level for two years). Hb. 83%. W.B.C. normal now, but developed a transient leucopenia, once as low as 2200 per ml. during the summer months last year.

Total serum, protein 8.5 g./100 ml., albumin 3.2, globulin 5.3.

Paper electrophoresis shows the elevated serum proteins are due entirely to a diffuse increase in the gamma globulins. No cryoglobulins or macroglobulins have been detected and no significant amounts of cold agglutinins have been demonstrated.

Urine and renal function tests appear normal now.

Case for Diagnosis (? Mycosis Fungoides).—Dr. I. McCALLUM.

A man aged 44.

History.—He was wounded by machine-gun fire in February 1942, and was

operated on for a ruptured liver. He was captured by the Japanese and was discharged from hospital one week after the operation. The wound broke down and was left to heal spontaneously. An incisional hernia then appeared and this was repaired surgically and remained soundly healed. The patient was in a P.O.W. camp for three and a half years and was repatriated in 1945. The operation wound started to break down in 1954 and has been discharging ever since.

Examination.—There is extensive ulceration of the anterior abdominal wall with surrounding induration and erythema.

Investigations (1958).—Urine, faeces, full blood count, E.S.R., liver function test, serum proteins with normal limits. W.R. and Kahn negative. Biopsy: "Microscopic examination shows a granulomatous lesion with numerous foreign-body giant cells which vary in size and are frequently vacuolated. Clefts are present in the fibro-muscular tissue with scanty fat cells and occasional remnants of muscle fibres. A few follicle arrangements are seen by no tubercle bacilli were demonstrated in the Ziehl-Nielsen preparation." Biopsy (1960). "Sections show the dermis to be replaced by granulation tissue heavily infiltrated with lymphocytes, together with occasional plasma cells, eosinophils and histiocytes. Beneath an area of ulceration there is an admixture of polymorphs. One or two giant cells were seen, but these are solitary and not related to any apparent foreign material, such as silica. The appearances are consistent with a chronic inflammatory granuloma."

Treatment (May 1958).—A course of tetracycline for eight days. Following this there appeared to be a distinct improvement.

Progress.—The condition has remained more or less unchanged since the patient's discharge from Roehampton in May 1958. He was referred to Dr. McCallum 21.i.60.

The opinion of the meeting was that this was a case of mycosis fungoides.

Manchester, 10 May 1960.

Lupus Erythematosus with Lichenoid and Mucosal Lesions.—Dr. G. AUCKLAND.

A joiner aged 44.

History.—Onset 7 months ago of bluish-red thickened scaly patches on the back of the left index finger. Gradual spread of similar lesions to the backs of most of the fingers, backs of the hands and ears. About 2 months ago, three bright red fixed patches appeared on the nose. General health not affected. No treatment has yet been given.

Examination.—Nose: three red patches of typical chronic discoid lupus erythematosus. Ears: bluish discoloration, infiltration and hyperkeratosis involving most of the pinnae. Hand and fingers: infiltrated, verrucose, bluish red patches on the backs and sides of most fingers, especially marked on the index and middle fingers. On the backs of the hands several smaller patches and papules, slightly verrucose, closely resembling lichen planus. Right forearm: a single lichenoid papule. Mucosa: the soft palate is covered with red, pinhead-sized macules. On both sides of the inner surface of the cheeks opposite the lower molars are white, lace-like patches, identical with those of lichen planus.

Investigations.—Blood count normal. No L.E. cells in peripheral blood. Slight increase in β globulins.

Histology.—A verrucose papule was excised from the back of the left hand which was reported as follows. "Hyperkeratosis with one follicular plug. A small area of basal liquefaction in one part of the epidermis. Some oedema of the corium and lymphocytic infiltration around blood vessels is present. The appearance is consistent with lupus erythematosus".

Postscript.—13 June 1960. After 1 month's treatment with tab. chloroquin sulphate 200 mg. b.d. there has been a dramatic improvement in all the lesions

the L.E. patches on the nose have faded considerably; the hyperkeratosis and bluish discoloration of the ears has disappeared leaving some brown pigmentation only; the verrucose, lichenoid, lesions on the fingers, hands and right forearm have become smoother, less infiltrated and paler, the mucous membrane lesions are now only just discernible. Further sections cut deeper into the original biopsy specimen showed appearances reported as follows. "Hyperkeratosis with one follicular plug. There is some liquefaction degeneration of the basal layer and irregular lengthening of the rete pegs with a 'saw tooth' appearance.

"A heavy lymphocytic infiltrate is present in the upper part of the corium. The appearance resembles lichen planus."

Dermatitis Herpetiformis with Eosinophilia.—Dr. J. CURRY.

A woman aged 39.

History.—Three weeks after a trivial burn she developed intense, generalized irritation and a bullous eruption over the whole body. A white blood count showed 12,800 w.b.c.s per c.mm. with 53% of eosinophils.

Treatment with steroids and antibiotics produced a remission of the bullous eruption and a return of the white cell count to normal. A month later the eruption re-occurred and the white cell count rose again to 42,900 with 44% eosinophils. This exacerbation lasted eight days and was controlled by sulphapyridine 1 g., and prednisolone 40 mg. daily. The prednisolone was gradually withdrawn and after three months her skin was clear on a maintenance dose of sulphapyridine 1 g. daily. Two weeks later, a further relapse occurred.

Mucha-Habermann Syndrome (Parapsoriasis Varioliformis).—Dr. P. B. MUMFORD.

A man aged 63.

History.—Three years' duration. The face and shoulders are mainly affected, though the knee has been involved on one occasion. The primary lesion is a slowly developing, intensely irritable papule. A lesion may clear without ulceration over a period of weeks or may break down in a "chancreiform" manner. Obvious sepsis and suppuration does not occur. The patient has periods of complete freedom for weeks on end.

Bacteriology.—Nasal swab gave a free growth of haemolytic *Staph. aureus*.

Treatment to eradicate any infective element by routine cleansing and to build up resistance by autogenous vaccine has proved valueless. W.b.c. 11,600 per cu.mm., neutrophils 68%, lymphocytes 26%, monocytes 4%, eosinophils 2%. Platelets abundant.

Behçet's Syndrome with Nail Changes.—Dr. B. PORTNOY.

A woman aged 38.

History.—Two years' history of a painful ulcer of the vulva. Biopsy carried out by a gynaecologist suggested an inflammatory reaction compatible with aphthous ulceration. In 1958 the labia minora were excised because of extensive ulceration. A month afterwards she developed swelling of the face, painful mouth ulcers and sore eyes. The vulval ulcer also recurred.

Past history.—Recurrent urticaria for 5 years due to aspirin sensitivity.

Examination.—March 1959, showed blepharitis, corneal ulceration and ulcers of the palate, buccal mucosa and vulva.

Treatment.—Triamcinolone 4 mg. *t.i.d.* was given with some improvement, though new ulcers continued to occur. At this time, all her toenails became thickened and friable. Scraping was negative for mycelium and a short course of griseofulvin made no change in their appearance.

The appearance of the toenails in May 1960 was similar to that in keratoderma blennorrhagica.

BOOK REVIEWS.

DISEASES OF THE NAILS.*

THE third edition of Pardo-Castello's *Diseases of the Nails* will be welcomed by younger dermatologists as it is the only work in the English language entirely devoted to nail disorders. This edition follows largely the pattern of the earlier editions and in general adds little. It is a clinical account of diseases as they affect the nails and is a review of much of the existing literature on nail disorders. In particular Heller's German text is freely quoted and Lewis's recent work on the anatomy of the nail is briefly described. It is a disappointment to find so little evidence of any investigative work on the causes of nail changes in the various conditions described. This is undoubtedly due to the difficulty of obtaining adequate biopsies of the nail matrix from living subjects. The photographs form an important part of the work and most are very good but at times one would prefer a close up view of a single nail in place of a somewhat distant view of several.

P. D. S.

DIFFERENTIAL DIAGNOSIS OF YAWS.†

THIS book is the continuation of *An International Nomenclature of Yaws Lesions*, also by Dr. Hackett, published in 1957 as World Health Organisation Monograph No. 36 which was reviewed in this journal (*Brit. J. Derm.*, 70, 262). It is essential to use both books together and the book under present consideration is cross-referenced to the previous volume.

The two books together constitute the most valuable aid to the clinical diagnosis of yaws yet published. Order has been brought out of the chaotic terminology, both of yaws and of the confusing plantar and palmar lesions so commonly encountered in tropical dermatology. The illustrations are an important feature in both volumes. They are of commendable clarity, with one exception. In the volume under review, Fig. 11 depicts a close-up view of pityriasis rosea, which, admittedly, must be a difficult subject to photograph and reproduce. It will not be so to a dermatologist, but is likely to be confusing to those doctors engaged in the mass treatment of yaws, for whom the book is primarily intended.

The sudden gross increase in the number of negroes permanently residing in this country during recent years has brought tropical dermatology sharply into focus for many dermatologists. As latent early yaws may persist up to five years, it is not surprising that cases of early cutaneous yaws are appearing in school children from endemic areas. For those faced with such cases, and with possible manifestations of late yaws in older patients, this book and its predecessor are indispensable. Both authors and publishers are to be congratulated for these easily handled, well produced and timely volumes.

H. E. B.

* *Diseases of the Nails*. V. PARDO-CASTELLO and O. A. PARDO (1960) 3rd ed. Oxford: Blackwell Scientific Publications. Pp. 284, 113 illus. Price £3 8s.

† *Differential Diagnosis of Yaws*. C. J. HACKETT and L. J. A. LOEWENTHAL (1960). Geneva: W.H.O. Monograph Series No. 45. Pp. 88. Figs. 52. Price 17s. 6d.

THE YEAR BOOK.*

THIS most comprehensive review has now dropped the word "syphilology" from its title, a change in keeping with that of the *British Journal of Dermatology*, which altered its title in 1951.

The number of valuable articles and reports appearing in the numerous journals now available, increases rapidly. While just as important as ever to keep up with new developments, it becomes increasingly difficult to do so. The tendency therefore, is to follow a few lines of interest thus perhaps missing valuable information elsewhere. For this reason, the enormous value of this book lies in its happy combination in summary form, of useful articles for revision and of those which may all too easily have been missed.

This year, the well-balanced leading article is on acne vulgaris. Many dermatologists will be glad to see that the authors are very guarded in their assessment of the value of progesterone therapy, and recommend caution in prolonged use of the sulphonamides, and in the use of chloramphenicol. It is interesting to note that a dose of 1000 r superficial x-rays (H.V.L. 0.7-1.0 mm. Al) is considered safe, as half that amount is usually considered to be both adequate and safe in this country.

Further interesting reports include a case of vitiligo of the scalp, occurring three weeks after a shock, followed by vitiligo of the body seventeen months later, and one describing alteration of the hair bulb in disorders of the thyroid gland.

A comparison of the ten commonest disorders seen at the beginning and end of a twenty-five year period, shows little essential change. In a case of erythema gyratum repens, discovery of a small hard painless lump in the breast and its removal, was followed by recovery of the skin condition. Three reports describing outbreaks of tinea capitis due to *T. violaceum*, black dot tinea capitis, and tinea due to *T. verrucosum*, indicate the necessity for remaining aware of the tinea problem.

Apart from the very comprehensive section on therapy, which includes interesting articles on such divergent subjects as griseofulvin and hypnosis for warts, there are among others, extensive sections on eczema, urticaria and investigative studies, a short but interesting one on drug reactions, and a miscellaneous section, where some varied clinical "oddities" may be found. A useful book and good investment.

G. B. M. H.

PHYSIOTHERAPY OF LEG ULCERS.†

THIS small book gives details of various methods of physiotherapy available in the treatment of chronic leg ulcers. It should be of value to both student and practising physiotherapist and gives the medical man not familiar with the subject some idea of the variety of methods used in this field.

In the reviewer's own ulcer clinic the nursing staff, the special departments for investigation, the physiotherapy department and the supplies department (for elastic stockings etc.) are all called in to help as thought necessary by the doctor in charge of the patient. It seems strange to meet the implication in this book that the charge of the patient's treatment should be taken over by the physiotherapist.

It seems odd too, that though we read of Bisgaard's bandage, and although firm deep massage is mentioned, no acknowledgement to Dr. Bisgaard's pioneer work is made and no reference to his book is given. The statement that "for many years

* *Yearbook of Dermatology* (1959-1960). Edited by R. L. BAER and V. H. WITTEN. Chicago: Year Book Publications. Pp. 479, 59 illus. Price \$9.00.

† *Circulatory Ulcers: A Physical Approach*. H. G. TRANCHELL and C. R. BANNISTER. (1960). Bristol: Wright. Pp. 91, 16 illus. Price 12s. 6d.

before the work of Bisgaard, Dickson Wright, and others, ulcers were considered to be incurable" is untrue as a reference to the history of this condition will show.

The book is well published and well printed.

S. T. A.

ADVANCES IN DERMATOLOGY.*

THIS book consists of lectures given at a course on advances in dermatology and venereology held at the Munich university clinic in 1959. Most of the authors were then working there, but distinguished contributors from outside Germany include Profs. Miescher, Jadassohn and Woringer and Dr. Walter Lever. The first 79 pages are largely devoted to theoretical and practical aspects of eczema. There are also chapters on subcorneal pustular dermatosis, reticuloses, sarcoid, lupus erythematosus, aphthous stomatitis and diseases of the hair and nails. There is only brief mention of griseofulvin as little experience of its use had been gained at the time of writing. Schirren contributes articles on the choice of adequate qualities of x-rays in the treatment of dermatoses, and on protection against the hazards of radiation. Those who race optimistically to the chapter on warts in the hope of finding major therapeutic advances will be disappointed. They may be consoled by the statement that at the Strasbourg clinic, the percentage of new patients with warts rose from 7.1% in 1955 to 14.9% in 1958. Most of these papers can be recommended as succinct and readable accounts of progress in fields of interest.

P. J. H.

THE FRENCH ENCYCLOPAEDIA†

THIS is the second issue of this encyclopaedia in its new form which will eventually cover the whole of dermatology in a comprehensive fashion. This volume deals with biochemistry of enzymes of the skin and water and electrolytes of the skin. Epidermomycosis follows and here we cannot quite agree that griseofulvin is effective in all superficial infections.

There are other chapters on Leishmania, cutaneous atrophies, tropical ulcers, naevi, etc. Some articles are based on morphological similarities and contain, as a result, a heterogeneous assembly, e.g. variola, acrodermatitis continua and syphilis in that on non-follicular pustules. The most comprehensive one deals with nodular *dermohypodermes*. There are some excellent coloured plates and a fairly widely drawn bibliography. These volumes should be available in every dermatological department as an up-to-date survey of French views.

F. F. H.

JOURNAL OF THE INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY.‡

THE launching of a new quarterly will scarcely raise a cheer from those of us who for years have been struggling unsuccessfully to keep our heads above water in the ever rising flood. Do we really want another journal? The answer is probably yes.

Sabouraud's work was a classic example of the way in which a clinician might contribute something of value to science, and the first number of *Sabouraudia* reveals

* *Fortschritte der praktischen Dermatologie und Venereologie, III*. Edited by A. MARCHIONINI (1960). Berlin: Springer. Pp. 312. Price DM 27.

† *Encyclopédie Médico-Chirurgicale* (1960). Vol. 38, Dermatology. Paris: Editions Techniques.

‡ *Sabouraudia*. Edited by J. C. GENTLES. Edinburgh: E. and S. Livingstone. Price £1 per quarterly issue.

the same process : the papers are well chosen to illustrate the effect of the impact of field worker or clinician on the laboratory work and *vice versa*, a happy interchange which has already borne fruit. The journal also provides a channel for publications that might otherwise be scattered about in clinical and biological journals and therefore easily overlooked.

The editor is Dr. J. C. Gentles, of griseofulvin fame. He is to be congratulated first on being singled out for the task of producing an international journal in Great Britain ; second for the attractive format and high quality of the presentation ; and, still more important, for the choice of subjects which, because of their practical slant, are likely to attract wide attention from clinicians, veterinarians and biologists. Human and animal mycology focuses attention on that most important aspect of disease, the host-parasite relationship. Knowledge is rapidly advancing on a wide front, and through this journal some of the advances will be made known throughout the world.

C. H. W.

CURRENT LITERATURE.

HERPES SIMPLEX FOLLOWING DECOMPRESSION OPERATIONS FOR TRIGEMINAL NEURALGIA. KENNETH H. BURDICK, JOHN R. HASERICK and W. JAMES GARDNER. (1960) *Arch. Derm., Chicago*, **81**, 919.

Approximately one third of 148 patients operated on intracranially for trigeminal neuralgia developed herpes simplex on the skin supplied by the nerve operated on. Herpes only follows operations on the intracranial portion of the nerve and never those on its peripheral branches. The local use of hydrocortisone preparations with or without antibiotics did not modify the attack rate. J. K.

THE HISTOGENESIS OF NAEVOID TUMOURS OF THE SKIN : THE FOLLICULOMA—A HAIR-FOLLICLE TUMOUR. ALBERT M. KLIGMAN and HERMAN PINKUS. (1960) *Arch. Derm., Chicago*, **81**, 922.

This apparently rare tumour is not recognizable clinically. It occurs in adults principally on the face and is usually single, though in one case hundreds of lesions were present on the head and trunk. The tumour is invariably small, ranging from 0.2 to 0.5 cm. in diameter. Histologically the tumour consists of a core, obviously a grotesque follicle, from which radiate strands or cords of epithelial cells which form hair follicles of varying degrees of atypicality. An essential component is an accompanying rich connective tissue stroma. J. K.

THE AMINO-ACID COMPOSITION OF EXFOLIATIVE TISSUE IN PSORIASIS. HUGO ZAHND and MARTIN CITRON. (1960) *Arch. Derm., Chicago*, **81**, 936.

The presence of 19 amino acids in psoriatic scales was determined quantitatively. Arginine and lysine were recovered in relatively high amounts compared with normal tissue, cystine and cysteine values were relatively low. The study was undertaken to see if it would give some clues as to the pathology of the disease but no conclusions are drawn. J. K.

CHANGES IN SERUM LIPOPROTEINS IN PSORIASIS.—EDWARD M. SHAPIRO, JOHN M. KNOX and SCOTT GRUNDY. (1960) *Arch. Derm., Chicago*, **81**, 940.

Thirty-one patients with psoriasis and 10 controls were used in this study. No detectable abnormality of systemic lipid metabolism was found in the psoriasis patients. The serum level of lipoproteins and cholesterol can be raised or lowered by diet and various forms of medical treatment but clinical improvement could not be correlated with these changes. J. K.

DERMATITIS WITH CAPILLARY FRAGILITY. KEMBLE GREENWOOD. (1960) *Arch. Derm., Chicago*, **81**, 947.

The marked similarity between Schamberg's disease and "khaki dermatitis" has been noted. Two components are required for the production of such a condition ; increase in capillary fragility and local irritation, such as is produced by a new wool shirt. This investigation shows that capillary fragility can be increased by sensitivity to oils used in the manufacture of woollen yarn, and that once this has happened, petechiae will tend to occur at points of injury and pressure, particularly on the legs due to gravitational factors. J. K.

FLAT CUTANEOUS XANTHOMATOSIS : A REVIEW AND CASE REPORT INCLUDING QUANTITATIVE FRACTIONATION OF SKIN LIPID. WILLIAM K. STEWART and OWEN A. FINN. (1960) *Arch. Derm., Chicago*, **82**, 1.

A 24-year-old male was found to be suffering from heart lesions of rheumatic origin, eunuchoidism, myasthenia, and multiple, flat, xanthomatous plaques which had been present since infancy. Any pathogenic relationship between these symptoms is uncertain. Three cases of flat xanthomata have previously been published, but the variable time of onset and inconsistent distribution of the eruption makes it uncertain whether they form a nosological entity. In the present case the plasma cholesterol level was normal but there was a generalized though moderate increase in skin sterol content. The authors present arguments to distinguish this case from histiocytosis X and

put in a plea for the use of the newer refined methods of lipid analysis of skin lesions to lead to a better understanding of the various xanthomatoses. J. K.

CHOLINESTERASE NAEVUS : CHOLINESTERASES IN PIGMENTED TUMOURS OF THE SKIN. R. K. WINKELMANN. (1960) *Arch. Derm., Chicago*, 82, 17.

Non-specific cholinesterase activity was found in all naevi with predominantly dermal components. It was most intense in neuroepithelial naevi. In junctional naevi such activity was not found in junctional tissue, but in compound naevi which had deep dermal elements some activity was shown in intermittent fashion. The cells of malignant melanoma or of blue naevi did not show cholinesterase activity. There was no apparent relationship between this enzymatic reaction and the tyrosinase-pigmenting reaction. In general there seems to be an inverse relationship to pigmentation and to malignant potential, and the reaction may have useful prognostic value.

J. K.

STATISTICAL SUMMARY OF 23,000 CASES OF DERMATOSIS SEEN OVER 12 YEARS.

H. REYNAERS. (1960) *Arch. belg. Derm. Syph.*, 16, 17.

This is an exhaustive summary of the dermatological cases seen in 12 years in a clinic in the industrial centre of Belgium. They formed 7.5% of the total patients who attended the Polyclinic; one third had allergic dermatoses, one third infectious dermatoses (including syphilis, 3.2% of the total) and the remainder various conditions. Psoriasis accounted for 2.1% of the cases—a percentage which approximates to that considered normal for the total population.

The various diseases are listed and considered as regards sex, age, seasonal influence and social position. J. K.

PHOTOSENSITIVITY DUE TO TETRACYCLINE DERIVATIVE. W. E. MORRIS. (1960) *J. Amer. med. Ass.*, 172, 1155.

Four days' medication with demethylchlortetracycline followed by intense sunlight provoked erythema and oedema of the exposed areas in a 30-year-old woman. Subsequently the drug alone produced no reaction, until she again exposed herself to sunlight. G. C. W.

LIGHT SENSITIVITY DUE TO DEMETHYLCHLORETETRACYCLINE. M. S. FALK. (1960) *J. Amer. med. Ass.*, 172, 1156.

Of 27 patients receiving this new tetracycline derivative, 4 showed sensitivity to sunlight with redness oedema and vesication, which took 2 to 3 weeks to subside. G. C. W.

CONTROLLED TRIAL OF METHOXSALEN IN SOLAR DERMATITIS OF CHIPPEWA INDIAN. R. R. SCHENCK. (1960) *J. Amer. med. Ass.*, 172, 1134.

The Chippewa Indians of Minnesota commonly get a seasonal dermatitis of the face and neck from exposure to sunlight. Patients who took two 10 mg. capsules of Methoxsalen daily fared worse than controls. G. C. W.

TREATMENT OF DERMATOSES WITH INTRAVENOUS METHYLPREDNISOLONE SODIUM SUCCINATE. L. C. GOLDBERG and J. R. BARKOFF. (1960) *J. Amer. med. Ass.* 172, 1514.

This report is based on the treatment of 242 patients with various dermatoses, using methylprednisolone sodium succinate intravenously. A daily dose of from 20 to 90 mg. was given over a three-week period. The various dermatoses responded well to this treatment and it is claimed that the side effects were less than with oral corticoids. G. C. W.

SUBUNGUAL HAEMORRHAGE IN PAN WASHERS. P. I. LONG. (1960) *J. Amer. med. Ass.*, 172, 916.

Tenderness of the finger tip together with haemorrhage under the nail plate is met with in kitchen workers. The condition is liable to occur if the work is traumatizing (scrubbing pans with wire wool), particularly if detergent solution gets into the finger of the protective rubber gloves. G. C. W.

ECZEMA DUE TO SUBSTANCES OF KNOWN CHEMICAL COMPOSITION. W. JADASSOHN. (1960) *Acta allerg., Kbh., Suppl. VII*, 185.

In eczema the epidermis and dermis react independently. The dermal reaction is transmissible but not the epidermal. Sensitization is not necessarily permanent. H. T. H. W.

A CLINICAL STUDY OF SENSITIVITY TO LOCAL APPLICATIONS. EDWIN SIDI. (1960) *Acta allerg., Kbh., Suppl. VII*, 196.

Sensitivity to streptomycin occurred in 7.5% and to PAS in 10.5% of tuberculous patients treated with these drugs. Nine out of eleven patients were desensitized to streptomycin and nine out of fifteen cases to PAS, steroid cover being used when necessary. Sensitivity to medicaments is one of the commonest causes of contact dermatitis. More attention should be paid to the sensitizing properties of new chemicals.
H. T. H. W.

EXPERIMENTALLY INDUCED PHOTOALLERGY TO SULFANILAMIDE. K. SCHWARZ and M. SCHWARZ-SPECK. (1960) *Acta allerg., Kbh., Suppl. VII*, 224.

A low catalase value is found in the blood of guinea pigs sensitized to light. *In vitro* experiments suggest that photodynamically active substances inhibit catalase.
H. T. H. W.

OBSERVATIONS ON ALLERGENICITY OF SIMPLE INORGANIC COMPOUNDS. H. STORCK and M. SCHWARZ. (1960) *Acta allerg., Kbh., Suppl. VII*, 2321.

A similarity of chemical constitution and electronic configuration was found in seven inorganic chemicals capable of sensitizing the skin.
H. T. H. W.

DRUG SENSITIVITY. SLOBODAN VUKOBRATOVIC. (1960) *Acta Allerg., Kbh., Suppl. VII*, 243.

Sensitivity to medicaments takes various forms. Liberation of histamine is responsible for anaphylactic phenomena which may be so intense that great caution must be observed in intra-dermal and scarification testing.
H. T. H. W.

OUR EXPERIENCE OF DRUG SENSITIVITY. V. DANILOVIC and M. LJALJEVIC. (1960). *Acta allerg., Kbh., Suppl. VII*, 250.

Sensitivity to medicaments, particularly penicillin, tends to increase. Most of the reactions are cutaneous, but other organs may be affected. The incidence is highest among women and among those in the 30-50 age group.
H. T. H. W.

NYLON DERMITITIS. G. E. MORRIS. (1960) *New Engl. J. Med.*, **263**, 30.

Dermatitis caused by nylon products in seven wearers is described. In six of them a patch test with virgin nylon was positive.
A. D. P.

PSEUDOMONAS INFECTIONS IN INFANTS AND CHILDREN. L. D. ASAY and R. KOCH (1960) *New. Engl. J. Med.*, **262**, 1062.

Infection with *Pseudomonas pyocyanea* became increasingly common in a childrens' hospital between 1952-1957 and increasingly difficult to control. Characteristic lesions in the skin were greenish pustules which ruptured and developed into punched out ulcers. The most useful antibiotics were polymixin, oxytetracycline, tetracycline and streptomycin, in that order.
A. D. P.

A CASE OF PRIMARY CUTANEOUS LISTERIOSIS. C. R. OWEN, A. MEIS, J. W. JACKSON and H. G. STOENNER. (1960) *New Engl. J. Med.*, **262**, 1026.

Thirty-six hours after attending an aborting cow, a veterinary surgeon felt ill. Next day discrete, tender, red papules appeared on his right arm and left wrist, some of which became pustular.

Listeria monocytogenes, sensitive to sulphonamides, was isolated from the lesions and also from the calf.
A. D. P.

ECZEMA VACCINATUM AS A COMPLICATION OF KERATOSIS FOLLICULARIS. W. GERSTEIN and W. B. SHELLEY. (1960) *New Engl. J. Med.*, **262**, 1166.

A man with keratosis follicularis developed Kaposi's varicelliform eruption after infection with vaccinia virus. Patients with extensive Darier's disease should be warned of the danger of infection with the viruses of vaccinia and herpes simplex.
A. D. P.

MULTIPLE NAEVOID BASAL-CELL EPITHELIOMA, JAW CYSTS AND BIFID RIB. A SYNDROME. R. I. GORLIN and R. W. GOLTZ. (1960) *New Engl. J. Med.*, **262**, 908.

Two patients are described with basal-celled epithelioma and cysts of the jaw; one had in addition a bifid rib. Four similar cases in the literature are mentioned and it is suggested the multiple naevoid epithelioma, cysts of the jaw and bifid ribs constitute a syndrome. A. D. P.

THE HOSPITAL NURSERY AS A SOURCE OF STAPHYLOCOCCAL DISEASE AMONG FAMILIES OF NEWBORN INFANTS. V. HURST and M. GROSSMAN. (1960) *New Engl. J. Med.*, **262**, 951.

The health of 94 families was investigated: their infants had been born sixteen months previously in a hospital nursery when there was an outbreak of impetigo. Many members of these families had developed skin diseases due to staphylococci, and the same organism as caused the original outbreak in hospital was frequently present. A. D. P.

PAPER ELECTROPHORESIS IN SERUM PROTEINS IN PEMPHIGUS FOLIACEUS. T. A. FURTADO and B. A. RODRIGUES. (1959) *J. invest. Derm.*, **33**, 227.

Hypoalbuminaemia and hypergammaglobulinaemia were constant findings in a series of 23 patients suffering from pemphigus foliaceus. The total protein concentration was almost within normal limits. A. J.

SOME FACTORS AFFECTING THE REACTION OF ALLERGIC CONTACT DERMATITIS. W. L. EPSTEIN and A. M. KLIGMAN. (1959) *J. invest. Derm.*, **33**, 231.

Pentadecyl catechol (PDC), 2-4 dinitrochlorobenzene (DNCB), paranitrosodimethyl aniline (NDMA), and Old Tuberculin were used as allergens in highly sensitive subjects. In addition, cantharidin and croton oil were used as primary irritants. Skin was removed for culture after sufficient time had been given for the *in vivo* conjugation of the allergen. Skin removed after 2, 4, and 6 hours' exposure to the allergens failed to show any reaction on culture. After leaving the skin for 24 to 48 hours after exposure to the allergens and then removing for culture histological changes became manifest. Artificial pressure designed to prevent the fluid moving into the epidermis during the development of a contact reaction prevented vesiculation. Nevertheless vesicles developed within 30 minutes of releasing the pressure. The authors therefore maintained that the vesicles were preformed during the contact reaction and the empty vesicles then became filled with fluid on release of the pressure. The damage is thought to be due to the lymphocytes and not fluid from the capillaries. A. J.

POLARIZATION OPTICAL STUDIES OF HYPERKERATOSIS, PARAKERATOSIS AND DYSKERATOSIS. D. A. ROE. (1959) *J. invest. Derm.*, **33**, 257.

Unstained skin sections were studied by polarization microscopy. In hyperkeratosis with an hypertrophic epidermis there was an increase of the birefringence. The author claims that psoriasis has a characteristic pattern of birefringence. A. J.

LIPOGENESIS IN HUMAN SKIN. J. F. PATTERSON and R. D. GRIESEMER. (1959) *J. invest. Derm.*, **33**, 281.

A method is described for the determination of lipogenesis in human skin. The epidermis synthesized sterols more readily than the dermis which appeared to be capable of manufacturing and storing squalene.

In psoriasis the incorporation of C^{14} with squalene and fatty acids was diminished while sterol formation was normal. The significance of these findings is not discussed. A. J.

THE NATURE OF CANTHARIDIN ACANTHOLYSIS. R. S. STOUGHTON and F. BAGATELL. (1959) *J. invest. Derm.*, **33**, 287.

These workers conclude that cantharidin induces enzymatic acantholysis. The enzymes activated appear to contain sulphhydryl groupings as pretreatment with sulphhydryl blocking agents such as ethyl maleimide, iodoacetic acid and ethyl thiosulphate all inhibit cantharidin acantholysis. It is also inhibited by hydrocortisone, alcohol, acetone, formalin, and freezing. A. J.

THE DIFFERENTIATION OF HUMAN FOETAL SKIN FOLLOWING HETEROTRANSPLANTATION. G. W. HAMBRICK and R. BLOOMBERG. (1959) *J. invest. Derm.* **33**, 177.

When foetal skin specimens were inserted into an everted hamster pouch, the embryonic skin survived and developed into adult epidermis with appendages. A. J.

AN ATTEMPT TO INDUCE "PIGMENT SPREAD" IN FRECKLED HUMAN SKIN. A. S. BREATHNACH. (1959) *J. invest. Derm.*, **33**, 193.

Freckles transplanted into pale skin of the same person did not spread. Neither did pigment extend into pale skin transplanted to a freckled area. These series of self experiments were therefore unfortunately unable to give us additional information on the mechanism of pigment spread. A. J.

THE COLLOIDAL STATE AS A STIMULUS FOR NON-ALLERGIC EPITHELOID GRANULOMAS : EXPERIMENTAL STUDIES IN MAN WITH PURE SODIUM STEARATE AND PALMITATE. H. J. HURLEY and W. B. SHELLEY. (1959) *J. invest. Derm.*, **33**, 203.

This paper deals with the experimental prevention of non-allergic granulomas. Test substances were injected intradermally in a dose of 0.1 ml. Of all the substances studied, the soaps, sodium stearate and sodium palmitate were greatly superior to other compounds in their ability to produce granulomas. It was also found that sodium stearate and sodium palmitate had the outstanding property of forming micellar colloidal systems. *In vitro* studies demonstrated that this property was responsible for their ability to induce granulomas. This colloid change occurs at the interface between the material and the tissue fluid or intracellularly after phagocytosis. The phagocytes filled with colloid have a high osmotic pressure and consequently became swollen.

The duration of these experimental granulomas is limited to the time required for their ingestion and metabolism ; this usually takes five weeks. These granulomas are not allergic, and should therefore be differentiated from allergic granulomas such as those caused by zirconium. A. J.

THE HUMAN HAIR CYCLE. A. M. KLIGMAN. (1959) *J. invest. Derm.*, **33**, 307.

Because human scalp hair grows for many years and rests briefly for a few months, the vast majority of the follicles are in anagen. Catagen occupies only a very short portion of the cycle ; this is a process of bulbar involution and cell loss. The melanocytes undergo simultaneous involution, and melanin synthesis ceases. The histological stages of catagen of human hair is described in detail. The summary of the author's observations is that catagen is a regression of the lower part of the follicle to a state resembling the embryonal epithelial germ. This later develops and gives rise to the next hair generation. A. J.

THE MECHANISM OF ACTION OF RUBEFACIENTS. G. P. FULTON, E. M. FARBER and A. P. MORECI. (1959) *J. invest. Derm.*, **33**, 317.

The mode of action of the esters of nicotinic acid and some essential oils was studied on preparations of the cheek pouch of hamsters.

Vasodilatation was produced by ethyl, methyl, n-hexyl and tetrahydrofurfuryl esters of nicotinic acid. These substances were applied to the arteriole walls by a micropipette. The vessels responding were the arterioles and the precapillary sphincters ; capillaries and non-muscular vessels did not react. The authors postulate a nervous mechanism, because a greater part of the vessel wall was affected than that to which the substance was applied. It is worthy of note that xylocaine abolished the vasodilatation response in 50% of the experiments. A. J.

EFFECTS OF X-RAYS ON SEBACEOUS GLANDS OF THE HUMAN FACE : RADIATION THERAPY OF ACNE. J. S. STRAUSS and A. M. KLIGMAN. (1959) *J. invest. Derm.*, **33**, 347.

Twenty-three males between the ages of 15 and 30 were given x-irradiation in varying doses of 300, 400, 800 and 1500 r in single exposures. Six were given 75 r per week for 12 treatments and eight were given 150 r per week for 12 weeks. Biopsies were then taken from these subjects at intervals (the HVL was 0.85 mm. Al.).

With a dose of 75 r weekly, it took 7-8 weeks before clinical improvement occurred, with 150 r weekly improvement occurred after 4 weeks. The maximum clearing effect however was not more than with the smaller dose. Single doses of 300 r had little effect ; 400 r gave moderate effects, and 800 r significantly reduced the size of the sebaceous glands. Return to normal size however occurred within 6 weeks.

The effect of x-ray therapy is mediated through sebaceous gland suppression. The best results were obtained with low dosage (75 r) given at weekly intervals over prolonged periods, up to a total dose of 1200 r. A. J.